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RESPIRATORY CARCINOGENICITY OF DIESEL FUEL EMISSIONS

By

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An experiment was carried out to compare the carcinogenicity of diesel exhaust particles (administered by fifteen weekly intratracheal instillations) to that of organic extracts of diesel particles, coke oven emissions, roofing tar condensate and cigarette smoke condensate. Appropriate solvent controls, untreated controls and positive controls were included in the design of the experiment. The overall incidence of respiratory tract tumors in any of the treatment groups was not significantly higher than in control hamsters. Similarly, there were no significant differences in the survival rates of hamsters treated with test materials from those of their respective controls. Hamsters treated with test materials generally showed significantly lower mean body weights than control animals. Treated hamsters generally showed a delay in time to reach maximum body weight when compared to hamsters in control groups. Treatment of hamsters with test materials induced a variety of hyperplastic, proliferative and inflammatory lesions of the respiratory tract. The highest incidence rates and greatest severity of the lesions were induced by diesel exhaust particles and coke oven emissions. Diesel exhaust extract and benzo(a)pyrene were less reactive, and cigarette smoke condensate and roofing tar volatiles produced the lowest incidence of respiratory tract lesions.

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FOREWORD

This report, IITRI No. L06138-10 (Final Report) describes studies conducted by the Life Sciences Department, IIT Research Institute for the U.S. Environmental Protection Agency during the period of September 1, 1979 through June 30, 1984. The studies were carried out under EPA Cooperative Agreement No. R806929. The project was initially monitored by Dr. Donald E. Gardner and later by Dr. Judith A. Graham of EPA's Health Effects Research Laboratory.

Alan Shefner served as Principal Investigator and the project directors for day-to-day activities were Dr. Bobby Collins and Dr. Carol Thompson. Mr. L. Dooley served as laboratory supervisor and he was assisted by E. Cichocki, C. Nicholes, N. Phee, J. Sutton, J. Dropkin, K. Ross, and J. Nafis. Dr. Arsen Fiks served as program pathologist. Ms. Jean Graf prepared all dosage forms of test materials used in the program and Dr. Walter Eisenberg carried out HPLC profile studies. Experimental data are recorded in IITRI Logbooks C24358, C24359, C24360, C24454, C24467, C24700, C24917, C24965, C24985, C24998, C25098, C25411, C25501, C25707, C26220, D2264, D2270, D2271, D2272, D2273, D2279, D2280, D2281, D2298, D2312, and D2346.

Respectfully submitted,
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ABSTRACT

A large scale experiment utilizing 3000 hamsters was carried out to compare the carcinogenicity of diesel exhaust particles (administered by fifteen weekly intratracheal inctillations) to that of organic extracts of diesel particles, coke oven emissions, roofing tar condensate and cigarette smoke condensate. Appropriate solvent controls, untreated controls and positive controls were included in the design of the experiment.

The overall incidence of respiratory tract tumors in any of the treatment groups was not significantly higher than in control hamsters. Treatment with benzo(a)pyrene resulted in significantly higher tumor incidences, primarily evidenced as polyps in the trachea, lung, and larynx. Similarly, there were no significant differences in the survival rates of hamsters treated with test materials from those of their respective controls. Hamsters treated with test materials generally showed significantly lower mean body weights than control animals. This effect began during the 15-week treatment period and frequently lasted into the post-treatment holding period. Treated hamsters generally showed a delay in time to reach maximum body weight when compared to hamsters in control groups.

Treatment of hamsters with test materials induced a variety of hyperplastic, proliferative and inflammatory lesions of the respiratory tract. The highest incidence rates and greatest severity of the lesions were induced by diesel exhaust particles and coke oven emissions. Diesel exhaust extract and benzo(a)pyrene were less reactive and cigarette smoke condensate and roofing tar volatiles produced the lowest incidence of respiratory tract lesions.

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LIST OF ABBREVIATIONS

DP -- diesel particles
DE -- diesel extract
COE -- coke oven extract
CSC -- cigarette smoke condensate
RTE -- roofing tar extract
DPFO -- diesel particles plus ferric oxide
DEFO -- diesel extract plus ferric oxide
CSFO -- cigarette smoke condensate plus ferric oxide
COFO -- coke oven extract plus ferric oxide
RTFO -- roofing tar extract plus ferric oxide
BP -- benzo(a)pyrene
BPFO -- benzo(a)pyrene plus ferric oxide
DPOO -- diesel particles alone
DPSV -- diesel particle solvent
DPFS -- diesel particle plus ferric oxide solvent
DEFS -- diesel extract plus ferric oxide solvent
COFS -- coke oven plus ferric oxide solvent
CSFS -- cigarette smoke plus ferric oxide solvent
RTFS -- roofing tar plus ferric oxide solvent
CCON -- colony control
N -- within normal limits
L -- lesions present
M -- tissue not available
I -- tissue inadequate
P -- lesion present, no grade
LN -- lymph node
SG -- salivary gland

SECTION 1
INTRODUCTION

The purpose of this study was to assess the carcinogenic potential of diesel engine exhaust particulates and organic solvent extracts, and to compare their carcinogenicity to that of other combustion products of known epidemiologic significance. The comparison materials included roofing tar and coke oven emissions and cigarette smoke condensate. All materials and the proper controls were given to hamsters by intratracheal instillation (Saffiotti technique) for 15 weeks. Animals were sacrificed at 110 weeks of age (98-99 weeks on study) and gross and histopathological examinations were made.

Two papers resulting from work carried out under this Cooperative Agreement were presented at the International Symposium on Health Effects of Diesel Engine Emissions, held in Cincinnati, Ohio on December 3-5, 1979, and sponsored by the Health Effects Research Laboratory. These papers were published and are referenced as follows:

> Preparation and Characterization of Diesel Exhaust Particles for Biological Experiments. IN: Health Effects of Diesel Engine Emissions - Proceedings, EPA-600/9-80-057a, November 1980, Vol. 1, pp 82-92, Jean L. Graf.
>
> Carcinogenicity of Diesel Exhaust Particles by Intratracheal Instillation-Dose Range Study. IN: Health Effects of Diesel Engine Emissions - Proceedings, EPA-600/9-80-057b, November 1980, Vol. 2, pp 994-1011. A.M. Shefner, L. Dooley, A. Fiks, C.J. Grubbs, H. Rust and W.R. Richter.

An additional paper was presented at the EPA 1981 Diesel Emissions Symposium, Raleigh, North Carolina, October 5-7, 1981. This presentation was included for publication as follows.

Respiratory Carcinogenicity of Diesel Fuel Emissions - Interim Results. IN: Toxicological Effects of Emissions from Diesel Engines, J. Lewtas (ed.), pp 329-355, Elsevier Biomedical, New York, 1982. A.M. Shefner, B.R. Collins, L. Dolley, A. Fiks, J.L. Grafand and M.M. Preache.

The final results of this program which are described in this report are being prepared in a form suitable for submission to an appropriate peer-reviewed journal.

SECTION 2
CONCULSIONS

The results of these studies indicate that diesel particles with or without ferric oxide and diesel extract with ferric oxide were not carcinogenic for hamsters when given intratracheally at 5.0, 2.5 and 1.25 mg doses once a week for 15 weeks. Similarly, coke oven extract, cigarette smoke condensate or roofing tar extracts in mixture with ferric oxide were not carcinogenic at 5.0, 2.5 and 1.25 mg doses given over the same time period. Benzo(a)pyrene plus ferric oxide caused numerous polyps in the trachea and a few carcinomas in the lung and trachea, especially in the second replicate experiment.

The presence of diesel particles in the lung, pleura, and trachea did cause a high incidence of lesions in these organs. The lesions were generally mild to moderate in severity and were dose related. The lesions included inflammatory reactions, granuloma formation, fibrosis, adenomatous and papillary hyperplasia, squamous metaplasia, and particle accumulation in the lung. Particle accumulation and inflammatory reaction were seen in the trachea, larynx and pleura in addition to fibrosis and proliferation in the pleura. The presence of these lesions in the lung, pleura, and trachea did not appear to be life threatening over the time course of this experiment since there were no significant differences between the survival rates of the hamsters given the test articles and their respective controls.

SECTION 3
RECOMMENDATIONS

Concern over a postulated increase in the proportion and numbers of light-duty diesel engine powered vehicles in the total automotive fleet has provided the impetus to studies of potential health effects of an increase in emissions of carbonaceous particulate matter which might result. The U.S. Environmental Protection Agency has responded by sponsoring a number of studies to assess such impacts of which this program carried out at IIT Research Institute is one.

The design of this current study incorporated not only the evaluation of diesel emission particles as a potential respiratory carcinogen but also the ability to compare any effects produced to those of an organic solvent extract of the diesel particles and to other combustion products of known epidemiologic significance. These other materials included for comparability and ranking of relative health risks were coke oven emissions, roofing tar volatiles, and cigarette smoke condensate.

Under the conditions of this experiment (once weekly intratracheal administration of test materials for 15 weeks and termination at two years) none of the test materials were carcinogenic. The positive control comound, benzo(a)pyrene, induced tumors, primarily polyps, in a significant proportion of treated hamsters using the same treatment regimen.

However, the absence of carcinogenic response to diesel particles and the other test substances under the conditions of this experiment and in the test species utilized does not permit definite conclusions with regard to their lack of carcinogenicity to human beings. The limitations on the total dose which can be effectively administered, the limited life span of the hamsters as test species, total number of animals treated, and possible species differences in sensitivity all mitigate against definitive conclusions. The lack of reported tumor induction in long-term experiments in which test animals have been exposed to diesel exhaust particles by the inhalation route is in agreement with the results of this study.

The instillation of diesel exhaust particles, with or without admixture of Fe_2O_3 carrier particles, produced inflammatory and proliferative responses in various portions of the respiratory tract. These responses were similar in degree to those induced by exposure to coke oven emissions and more severe than those induced by diesel particle extracts, roofing tar volatiles, and cigarette smoke condensate.

While the induced respiratory tract pathology did not affect survival rates in otherwise unstressed hamsters, the effects of diesel particle exposure on the ability of animals to respond to other stressors should be evaluated. Intratracheal administration with diesel particles provides a useful method for loading the respiratory tract of test animals with known and reproducible burdens. Measures of effect which could have significance for public health include:

- Respiratory function under work or exercise stress.
- Reduction in immunocompetence.
- Additive effects in individuals with reduced respiratory function.
- Long-term consequences of the deposition of diesel particles for which longer lived test species would be necessary.
- Cocarcinogenic properties of diesel particles.

SECTION 4
MATERIALS AND METHODS

TEST ARTICLES

Definition

The materials used in the study were diesel engine emission particles, organic solvent extracts of the diesel particles, extracts of roofing tar volatiles and coke oven emissions, and cigarette smoke condensate. With the exception of diesel particles, all test materials were admixed with an equal weight (w/w) of ferric oxide. The specific test materials were defined as follows:

Diesel Particulates - filter collected (DP)

Diesel Extract - dichloromethane extract of diesel particulates (DE)

Coke Oven Extract - dichloromethane extract of coke oven particles (COE)

Cigarette Smoke Condensate - suspended in acetone (CSC)

Roofing Tar Extract - dichloromethane extract of roofing tar particles (RTE)

The diesel particulates and extracts, coke oven extracts, and roofing tar extracts were received from the Environmental Protection Agency (EPA), Research Triangle Park, NC. The cigarette smoke condensate was received from Oak Ridge National Laboratory. All materials were stored at -70°C (stock solution) or at -15°C (working solutions) until used. Table 1 shows the identifying information supplied with each material and the quantities received.

Table 1
Raw Materials Selected For Use

Material	Identifying Information on Container	Date Received	Container(s) X Amount	Amount Needed 15 Weeks
Diesel Particles-1	Run Nos. 9490-9492; 9496 -9509 9533-9539; 9578 November 1979 1978 Olds 350 Diesel	12/5/79	1 x 64.3g	35g
Diesel Particles-2	Run Nos. 9533-9539; 9578 November 1979 1978 Olds 350 Diesel	12/5/79	1 x 78.8g	35g
Diesel Extract	Run Nos. 9490-9588 HWFET 1978 Olds 350 0.0709 g/ml methylene chloride (250ml) December 1979	12/13/79	4 x 17.6g	35g
Coke Oven Extract	"Contains ~ 77g coke oven tar in methylene chloride"	1/23/80	1 x 77g	13.2g
Cigarette Smoke Condensate	EPA/ORNL CHEM. REPOSITORY Sample No. 6201.164 30g in 200 ml Acetone	4/10/79	1 x 30g	13.2g
Roofing Tar Extract	"2nd Asphalt Extract" 200 mg/ml, 100 ml methylene chloride	5/15/79	4 x 79g	13.2g

Preparation

With the exception of diesel particle suspensions, all emulsions were prepared weekly, the day before they were required for use. The diesel particle suspensions were prepared once every three weeks due to limited amounts of test material, and the requirements of the specific mixer.

The following paragraphs contain brief descriptions of the preparation of the test articles. The detailed description of methods used in preparation of these materials is provided in Appendix A.

Diesel Particles (DP) and Diesel Particles Plus Ferric Oxide (DP+Fe_2O_3) Suspensions: The whole particulate diesel emissions were received as a dry powder and stored at -70°C. Exhaust from several runs of the EPA'S 350 Oldsmobile diesel test engine were collected on single teflon coated glass fiber filters. The exhaust particles were than scraped from the filter surface to provide the loose powder supplied to IITRI.

Appropriate quantities of diesel particles were taken from the stock bottles once every three weeks to prepare the working solutions. Propylene glycol (10% w/v) was added to the weighed diesel particles. After hand-swirling saline containing 0.5% (w/v) gum arabic and 0.5% (w/v) gelatin was added to bring the suspension to the appropriate volume. The suspensions were mixed, transferred into storage bottles, and stored at -15°C until use.

The preparation of the diesel particles plus ferric oxide was the same as that for diesel particles except that after mixing ferric oxide was added to the suspension.

Diesel Extract Plus Ferric Oxide (DE+Fe_2O_3): Solvent extracts of whole particle diesel exhaust were provided to IITRI as solutions of the extracted material in dichloromethane. To prepare the working solutions, dichloromethane was removed from an appropriate volume before propylene glycol was added. The emulsion was heated at 70°C to allow liquification of the tarry compounds of the extract. The material was mixed for a short time before the saline-containing gelatin and gum arabic was added. Mixing continued until the emulsion achieved its lightest color (1 to 2 min.). Ferric oxide was mixed into the emulsion and the complete emulsion was poured into storage vessels.

Cigarette Smoke Condensate Plus Ferric Oxide (CSC+Fe_2O_3): The cigarette smoke condensate was received as a solution in acetone. The emulsion was prepared by using methods identical to those used for diesel extract.

Coke Oven Extract Plus Ferric Oxide (COE+Fe_2O_3): The extracts of coke oven emissions were received as solutions in dichloromethane. After aliquoting the extract solution into the mixing vessels, the solvent was blown off, and propylene glycol was added. The emulsion was mixed before hot saline-containing gelatin and gum arabic was added, and mixing continued until the emulsion attained its lightest color. The ferric oxide was then added and the final suspension was immediately transferred to storage bottles.

Roofing Tar Extract Plus Ferric Oxide (RTE+Fe_2O_3): Extracts of roofing tar volatiles were received in dichloromethane. The procedure for preparation of the roofing tar extract emulsions was similar to that used for the diesel extract. The major differences were the higher mixing speeds, and longer mixing times required for the roofing tar and the addition of ferric oxide before, rather than after, addition of saline.

Benzo(a)pyrene Plus Ferric Oxide (BP+Fe_2O_3): A 1:1 by mass mixture prepared by precipitating the benzo(a)pyrene onto ferric oxide served as a positive control.

Vehicle Controls

The vehicle control for the diesel particle exposure group consisted of physiological saline containing gelatin (0.5% w/v), gum arabic (0.5% w/v), and propylene glycol (10% w/v). Vehicle controls for exposure groups treated with test articles mixed with ferric oxide consisted of the saline solvent containing 5 mg of ferric oxide per 0.2 ml. The vehicle control for the benzo(a)pyrene exposure groups was saline without the propylene glycol and the ferric oxide concentration was 2 mg/0.2 ml saline.

ANIMALS

Male Syrian Golden Hamsters strain LAK;LVG, were purchased from Charles River Breeding Laboratories (North Wilmington, Ma.). The studies were carried out in two replicates. The first replicate involved 1470 hamsters and 1530 hamsters were used in the second. Hamsters in the first replicate were born between March 3 and 17, 1980 and were 6 to 8 weeks of age when received.

The hamsters in the second replicate were born between July 7 and 21, 1980 and were 6 to 8 weeks of age when received. The hamsters were kept in quarantine for a minimum of three weeks prior to being placed on study at approximately 12 weeks of age. Prior to being placed on study the hamsters were weighed and the mean body weight was determined. All hamsters whose body weight deviated from the mean by ±15%, and any that appeared unhealthy were discarded.

Each hamster was given a permanent identification number, consisting of holes, nicks, or a combination of both punched in either left, right or both ears. The left ear markings identified the numbers 1 to 9 (ones) and the right ear markings identified the numbers 10 to 300 (tens and hundreds).

The hamsters were housed in polycarbonate cages (18-1/2" x 10" x 8-1/2") suspended from racks on tracks and each level of rack was covered with filter sheets. The cages were changed once a week and the racks were changed every two weeks. All hamsters received *ad libitum* Wayne Blox and tap water. Fresh food and clean water bottles containing fresh water were provided at each cage change.

The hamsters were initially housed three per cage. However, due to continuing fighting, they were later housed two per cage separated by stainless steel dividers. The cage dividers were installed over a five week period (11/24/80 to 1/2/81).

TREATMENT GROUP ALLOCATIONS

The study design, which consisted of two replicate trials, was used because of the demands of experimental manipulation and statistical considerations. The allocation of treatment groups in the first and second replicate study is shown in Tables 2 and 3. The hamsters from each treatment group and their associated solvent controls were assigned to separate rooms. Cages were randomly assigned to specific locations on the racks in each room. Cages were identified as to dose level and individual animal numbers.

FREQUENCY AND ROUTE OF ADMINISTRATION OF TEST ARTICLES

A volume of 0.2 ml of the test or control material was instilled into the trachea of hamsters once a week for fifteen weeks by using the Saffiotti intratracheal instillation technique.

Table 2
Treatment Group Allocation, First Replicate

Treatment Group	Dose (mg/wk)	Sex	Number of Animals	12 Month Sacrifice Number of Animals	Total
Diesel Particle	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Solvent	0.0	M	50	10	60
Diesel Particle + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe O + Solvent	5.0	M	25	5	30
Diesel Extract + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe O + Solvent	5.0	M	25	5	30
Coke Oven + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe O + Solvent	5.0	M	25	5	30
Cigarette Smoke + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe O + Solvent	5.0	M	25	5	30
Roofing Tar + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe O + Solvent	5.0	M	25	5	30
Benzo(a)pyrene + Ferric Oxide	2.0	M	50	10	60
Colony Control	-	M	100	20	120
Total:			1,225	245	1,470

Table 3
Treatment Group Allocation, Second Replicate

Treatment Group	Dose (mg/wk)	Sex	Number of Animals	12 Month Sacrifice Number of Animals	Total
Diesel Particle	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Solvent	0.0	M	50	10	60
Diesel Particle + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe_2O_3 + Solvent	5.0	M	25	5	30
Diesel Extract + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe_2O_3 + Solvent	5.0	M	25	5	30
Coke Oven + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe_2O_3 + Solvent	5.0	M	25	5	30
Cigarette Smoke + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe_2O_3 + Solvent	5.0	M	25	5	30
Roofing Tar + Ferric Oxide	5.0	M	50	10	60
	2.5	M	50	10	60
	1.25	M	50	10	60
Fe_2O_3 + Solvent	5.0	M	25	5	30
Benzo(a)pyrene + Ferric Oxide	2.0	M	50	10	60
Gelatin saline Control	0.5	M	50	10	60
Colony Control	-	M	100	20	120
Total:			1,275	255	1,530

STATISTICAL METHODS

In the statistical analysis of these data three general types of data were considered: (1) body weights repeatedly measured in the same animals, (2) time to death (i.e., survival time), and (3) the presence or absence of a variety of histopathological lesions. The statistical analysis of body weight data involved (a) fitting a polynomial regression model of degree three to the temporal body weight curves for each group, (b) estimation of 95% confidence limits for each curve, and (c) a between group comparison of the entire time trend by graphical superimposition of the estimated trend line and confidence limits on the same chart. The degree of overlap of confidence bounds between treated and control animals provided a statistical test of the null hypothesis of no difference in body weight trend lines between groups.

The analysis of survival time data proceeded in two phases. First, a Cox regression model was fit using outcome (i.e., dead vs alive) as the dependent variable and replication, dose, compound and the dose by compound interaction as the independent variables. Second, individual pairwise comparisons (i.e., control vs low dose for compound 1) were obtained using product-limit estimations and both the Mantel-Cox and Breslow statistics were used to test for equality of survival distributions.

The analysis of histopathological data was performed using Chi-square statistics. These statistics were used to test the null hypothesis of no difference in the proportion of a specific lesion between treated and control animals.

QUALITY ASSURANCE

Quality assurance functions for the program were performed by the IITRI Quality Assurance Unit. During the course of the study all specimens, wet tissues, blocks and slides were catalogued. All slides and copies of histology verification sheets and organ checklists from necropsy were given to the pathologist for evaluation. Logs were maintained listing materials sent out to the pathologist and were checked upon return to assure all materials were included. All pathology data sheets were checked to assure proper data transfer for reporting purposes. Specimens and raw data generated during the course of the study will be retained in the IITRI Life Sciences Archives for a period of at least 8 years.

SECTION 5
EXPERIMENTAL PROCEDURES

CLINICAL OBSERVATIONS

Beginning with test week 1, the hamsters were observed daily in the mornings for abnormal signs. In addition, a mortality check was performed at least once daily usually in the afternoon. The hamsters were weighed once a week for the first 15 weeks and biweekly thereafter. A complete physical examination, including palpation for masses, was also carried out at this time. All observations and the date of their first occurrence were recorded for each individual hamster.

PATHOLOGY

Extensive necropsies were performed on all test and control hamsters that were either found dead or dying or in a moribund state, and on hamsters sacrificed at the scheduled interim and terminal sacrifices. The interim sacrifices occurred when the hamsters were one year old, during test weeks 42 to 43 and 41 to 42 for the first and second replicates, respectively. The terminal sacrifices occurred when the hamsters were 110 weeks old, during test week 97 for the first replicate and test weeks 98 to 99 for the second replicate.

The necropsy involved a thorough examination of all external surfaces, body cavities, and orifices. The brain, liver, heart, spleen, kidneys and testes of hamsters at interim and terminal sacrifices were weighed before fixation. The lungs were infused with 10% neutral buffered formalin and, together with the remaining tissues (except eyes and testes), were fixed and stored in formalin for no less than 48 hrs before processing. The eyes were fixed in gluteraldehyde and the testes in Bouin's solution for 24 hrs and then preserved in alcohol.

The tissues listed below were collected at necropsy. Tissues marked with an asterisk were processed by standard histologic techniques, stained with hematoxylin-eosin, and subjected to microscopic histopathologic examination.

Skin*
Mandibular salivary gland*
Mandibular lymph node*
Mammary gland*
Sternum*
Costochondral junction, rib
Thymus*
Thyroids and parathyroids*
Heart*
Esophagus*
Lung*
Larynx*
Trachea*
Thoracic lymph nodes*
Liver*
Gall bladder*
Adrenal glands*
Spleen*
Pancreas*
Kidneys*
Urinary bladder*
Testes*
Epididymes*
Seminal vesicles
Prostate*
Stomach*
Duodenum*
Jejunum*
Ileum*
Cecum*
Colon*
Rectum*
Mesenteric lymph node*
Skeletal muscle
Sciatic nerve
Ears
Eyes*
Nasal turbinate*
Brain*
Pituitary*
Spinal cord (thoracic
and lumbar)
Blood smear
Any other gross lesions*

A summary of gross observations found at the terminal sacrifices is presented by treatment group and for each replicate study in Appendix B. The incidence of microscopic lesions are summarized by treatment group, dose and replicate in Appendix C. The incidence of neoplastic lesions is presented by treatment group and replicate in Appendix D. A summary of gross and microscopic observations for the one year sacrifice is presented by treatment group and replicate in Appendix E. Reports of gross and microscopic findings for each individual hamster are maintained and available in IITRI project file archives.

The grading system and abbrevations used in the pathology tables are as follows:

N = Within Normal Limits
L = Lesions Present
Ñ = Tissue Not Available
I = Tissue Inadequate
P = Lesion Present, No Grade
LN = Lymph Node
SG = Salivary Gland

Glossary of Terms:

The terms used to describe the more common lesions in the target organs are as follows.

Lungs:

Particles - presence of test article and/or ferric oxide particles either free in the tissues or within alveolar macrophages.

Inflammatory reaction - presence of inflammatory cells, primarily mononuclear cells and neutrophils around particles.

Granuloma - Inflammatory reaction consisting of the accumulation of macrophages, lymphocytes, and plasma cells in the center of which is test material.

Adenomatous hyperplasia - proliferation of the epithelial cells of the bronchioles and bronchi with the formation of glandular or gland-like structures.

Papillary hyperplasia - proliferation of the epithelial cells of the bronchioles and alveoli with the formation of papillary structures.

Ciliary metaplasia - a lesion seen in connection with adenomatous hyperplasia; presence of metaplasia of the hyperplastic epithelial cells so that they become ciliated.

Squamous metaplasia - transformation of the alveolar and bronchiolar epithelium to stratified squamous epithelium.

Fibrosis - formation of fibrous tissue mainly in alveolar walls and around bronchi and bronchioles as observed with the light microscope.

Pleura:

Proliferation - hyperplasia of mesothelial cells of the visceral pleura.

Papillary structures - poliferation of visceral mesothelial cells with the formation of papillary structures.

Larynx and Trachea:

Glandular ectasia and cyst formation - dilatation of glands caused by the retention of glandular material.

Thoracic Lymph Node:

Lymphostasis - retention of lymph.

SECTION 6
RESULTS

BODY WEIGHTS

Body weight curves generated by fitting a polynomial regression model to actual data points as described under Statistical Methods were visually inspected for periods of time where the confidence bounds of treated group body weights did not overlap those of their respective controls. Table 4 shows the time periods expressed in weeks, over which such differences were observed for Replicate 1 and the direction of the difference (higher or lower body weight than controls). Table 5 shows similar information for the second replicate.

As can be seen from Tables 4 and 5 and from inspection of the regression curves included as Appendix F, hamsters treated with test materials generally tended to have lower body weights than did their respective control animals. This body weight difference frequently was first seen during the course of the 15-week treatment period and lasted well beyond the cessation of treatments. The only deviations from this response pattern were the hamsters treated with coke oven emissions in the second replicate and those treated with the high (5.0 mg) dose of cigarette smoke condensate also in the second replicate.

CLINICAL OBSERVATIONS

All observations and the date of their first occurrence were recorded for each individual hamster. The clinical observations were tabulated by treatment group at each dose level for the two replicate studies (Tables 6 and 7). The results indicated that the clinical observations were not treatment- or dose-related. Table 8 summarizes these data disregarding the treatment groups or dose levels and considering each replicate study separately. Thus, this table was used to compare the results obtained in the replicate studies. The table includes the clinical observations, and the total number of hamsters and the percent of hamsters showing specified clinical signs in the first and second replicate studies.

Table 4
Summary of Time Periods at Which Statistically Significant Body Weight Differences Were Observed, First Replicate

Compound[a]	Control[a]	Dose	Time Period (wks)	Direction		
DPOO	DPSV	5.0	3-29	L*	96-100	L
		2.5	-	-		
		1.25	51-67	H**	85-100	L
DPFO	DPFS	5.0	3-43	L	76-100	L
		2.5	76-100	L		
		1.25	-	-		
DEFO	DEFS	5.0	0-57	L		
		2.5	5-61	L		
		1.25	-	-		
CDFO	CDFS	5.0	27-100	L		
		2.5	33-89	L		
		1.25	51-81	L		
CSFO	CSFS	5.0	11-63	L		
		2.5	23-47	L	83-100	L
		1.25	21-47	L	77-100	L
RTFO	RTFS	5.0	85-100	L		
		2.5	79-100	L		
		1.25	81-100	L		
BPFO	CCON	2.0	5-72	L		
DPSV	CCON	----	36-75	L		

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[a] See page viii for definitions

* Test groups had significantly lower body weights than controls.

** Test groups had significantly higher body weights than controls.

Table 5
Summary of Time Periods at Which Statistically Significant Body Weight Differences Were Observed. Second Replicate

Compound[a]	Control[a]	Dose	Time Period (wks)	Direction		
DPOD	DPSV	5.0	0-100	L*		
		2.5	40-100	L		
		1.25	44-95	L		
DPFD	DPFS	5.0	11-39	L	65-90	H**
		2.5	16-39	L		
		1.25	-	-		
DEFD	DEFS	5.0	1-60	L	90-96	L
		2.5	2-50	L	64-94	H
		1.25	4-58	L		
CDFD	CDFS	5.0	6-76	H		
		2.5	8-56	H	74-100	L
		1.25	8-54	H	78-100	H
CSFD	CSFS	5.0	42-92	H		
		2.5	6-52	L	88-100	L
		1.25	12-22	L	72-84	H
RTFD	RTFS	5.0	10-44	L		
		2.5	4-98	L		
		1.25	-	-		
BPFD	GE	2.0	33-94	L		
DPSV	CCDN	----	5-96	L	91-100	H
GS	CCDN	----	-	-		

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[a] See page viii for definitions

* Test groups had significantly lower body weights than controls.

** Test groups had significantly higher body weights than controls.

Table 6
Clinical Observations. First Replicate

Clinical Observations	BP				BP+FD**				BB+FD				COE+FD				CBC+FD				RTE+FD				BP+FD 2 0	COLONY CONTROL
	H	M	L	S*	H	M	L	S	H	M	L	S	H	M	L	S	H	M	L	S	H	M	L	S		
Bleeding from tail	0	0	0	0	0	2	4	4	0	0	0	0	2	1	2	0	0	0	0	0	1	0	1	0	0	0
Ataxia	0	0	0	2	0	0	1	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	3
Dyspnea	1	1	4	3	4	5	4	1	2	3	4	1	5	4	1	0	6	7	2	4	2	2	6	3	2	8
Lethargy	2	1	3	4	4	2	2	0	0	5	4	1	1	3	1	0	1	5	4	1	1	1	3	1	3	6
Diarhea	0	1	0	0	1	1	2	1	0	0	2	1	2	0	2	0	0	1	1	0	1	0	3	0	0	1
Tremors	4	2	2	6	10	4	7	1	3	3	7	4	5	8	3	2	3	5	4	4	2	4	6	1	2	8
Convulsions	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Comatose	4	1	0	3	5	0	4	1	1	2	4	2	1	3	1	2	2	3	2	1	1	0	3	0	2	3
Bleeding from mouth	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Mass	2	1	2	2	1	4	4	1	3	0	1	0	2	1	1	1	2	3	3	1	2	0	1	2	3	3
Eye Discoloration	1	0	0	0	1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	2	4
Skin lesions or abscess	52	53	53	38	38	37	37	27	34	36	35	27	35	35	37	28	39	40	38	26	37	38	37	26	52	118
Swollen paw	1	2	2	3	0	2	0	1	0	1	0	0	1	0	0	0	3	0	0	2	0	0	1	0	0	0
Paralysis	0	0	0	0	0	1	0	1	0	0	0	0	1	0	0	0	1	0	1	2	1	0	0	0	0	0
Infected or closed eyes	13	13	12	15	15	8	16	8	14	10	17	7	11	10	8	8	11	16	14	11	12	13	19	5	13	29
Hairless	17	12	10	12	13	12	21	6	15	10	14	8	15	10	7	6	12	13	6	10	14	12	13	4	11	31
Edema	1	3	4	4	4	0	5	1	5	3	4	3	3	3	5	2	4	4	0	2	3	3	1	1	2	3
Unthriftiness	0	1	0	1	1	0	0	1	1	0	1	0	0	0	0	0	1	0	0	0	0	0	1	1	0	0
Swollen anus	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Prolapsed rectum	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0
Head tilt	1	0	0	0	1	1	1	1	1	0	0	1	1	2	0	0	1	3	0	0	0	2	0	0	1	1
Swollen abdomen	0	0	0	0	0	0	0	1	1	0	0	0	1	1	1	0	0	0	0	1	1	0	0	0	0	1
Total number of animals	60	60	60	60	60	60	60	30	60	60	60	30	60	60	60	30	60	60	60	30	60	60	60	30	60	120

* H = high dose, M = mid dose, L = low dose, S = solvent
** FD = Fe_2O_3

Table 7
Clinical Observations, Second Replicate

Clinical Observations	DP				DP+FO**				DE+FO				CDE+FO				CBC+FO				RTE+FO				BP+FO 2.0	COLONY CONTROL	GELATINE SALINE
	H	M	L	S*	H	M	L	S	H	M	L	S	H	M	L	S	H	M	L	S	H	M	L	S			
Bleeding from tail	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
Ataxia	0	0	0	1	0	0	0	0	0	0	1	0	1	0	0	0	3	0	0	0	0	0	0	0	0	1	0
Dyspnea	2	1	6	1	1	8	2	1	4	2	4	0	3	1	7	1	3	5	5	1	3	1	6	3	5	4	4
Lethargy	6	4	3	7	3	2	3	2	4	4	3	1	4	1	3	3	6	4	6	2	6	4	4	1	5	8	6
Diarhea	2	3	4	2	1	1	1	0	1	1	2	3	0	0	1	0	5	0	1	2	0	1	1	0	1	3	2
Tremors	6	3	5	6	1	3	5	1	3	1	0	1	5	1	6	1	8	1	5	2	5	3	5	0	4	6	4
Convulsions	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Comatose	3	1	0	1	0	1	2	0	3	1	1	0	1	0	2	0	0	2	0	0	1	1	0	2	1	2	3
Bleeding from mouth	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0
Mass	1	4	3	0	0	2	1	0	2	2	1	1	5	1	1	2	5	2	0	1	2	1	0	0	0	1	0
Eye Discoloration	1	3	2	0	1	0	2	2	1	1	2	2	1	2	2	0	1	1	2	2	3	1	0	0	[illegible]	2	0
Skin lesions or abscess	11	12	10	11	0	3	6	5	5	6	7	3	14	16	10	5	6	6	3	4	10	17	6	4	3	13	10
Swollen paw	0	0	0	0	0	0	0	0	0	1	0	0	2	0	2	0	4	7	4	6	0	0	0	0	0	16	12
Paralysis	0	1	0	1	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0
Infected or closed eyes	5	6	10	5	3	6	3	2	7	4	7	8	6	6	5	2	8	5	7	2	9	9	3	3	6	21	7
Hairless	19	17	13	18	7	14	17	9	19	18	17	8	14	13	15	10	13	11	12	8	16	16	11	8	8	40	16
Edema	6	3	5	6	4	3	6	2	8	12	6	3	4	5	4	3	8	6	7	1	4	5	5	3	7	16	9
Unthriftiness	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Swollen anus	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	2	0	0
Prolapsed rectum	1	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
Head tilt	2	2	4	2	2	2	1	1	1	5	1	1	3	1	0	1	2	0	0	0	0	1	3	0	1	3	1
Swollen abdomen	0	0	0	0	2	0	0	0	0	0	1	0	0	0	0	0	1	0	1	0	1	0	1	0	0	1	1
Total number of animals	60	60	60	60	60	60	60	30	60	60	60	30	60	60	60	30	60	60	60	30	60	60	60	30	60	120	60

* H = high dose; M = mid dose; L = low dose; S = solvent
** FO = Fe_2O_3

Table 8
Summary of Clinical Observations
First and Second Replicates

Clinical Observations	Number of Hamsters Involved			
	First Replicate		Second Replicate	
	Totals*	%	Totals**	%
Bleeding from tail	17	1	2	0
Ataxia	9	1	4	0
Dyspnea	85	6	72	5
Lethargy	56	4	106	7
Diarrhea	19	1	38	2
Tremors	100	7	91	6
Convulsions	1	0	0	0
Comatose	51	3	28	2
Bleeding from mouth	1	0	1	0
Mass	46	3	38	2
Eye discoloration	12	1	36	2
Skin lesion and/or abscess	1373	93	214	14
Swollen paw	21	1	54	4
Paralysis	10	1	5	0
Infected and/or closed eyes	323	22	116	11
Hair loss	314	21	387	25
Edema (subcutaneous)	70	5	147	10
Unthriftiness	9	1	3	0
Swollen anus	0	0	3	0
Prolapsed rectum	3	0	4	0
Head tilt	18	1	37	2
Swollen abdomen	8	1	7	0

* Total hamsters = 1,470
** Total hamsters = 1,530

When the clinical observations were compared between replicates, a significant difference was found in the percent of hamsters with skin lesions. In the first replicate 93% of the hamsters had skin lesions while only 14% had similar lesions in the second replicate. The skin lesions were caused by the fighting that occurred early in the experiment when the hamsters were housed in groups of three. This problem was solved by housing only two hamsters per cage and separating individual hamsters with steel dividers placed in each cage. The individual housing favored the hamsters in the second replicate because these hamsters were on the study for one month before the dividers were installed, while hamsters in the first replicate had been on study for five months. No other significant differences in clinical observations between replicates were observed.

SURVIVAL

Computer-generated curves of cumulative proportion of surviving hamsters plotted against survival time in months for high dose test groups and for their respective controls for the combined replicates are shown as Figures 1 to 6, in Appendix B.

These survival curves as well as those for middle and low dose groups, for benzo(a)pyrene, and for various comparisons between treated and untreated control groups are included as Appendix G. Where the comparison is between animals from only one replicate, such as in the case of gelatin-saline controls which were only included in the second replicate, the legend to the plot so indicates.

Two statistical analyses, namely Mantel-Cox and Breslow, were used to test for equality of survival distributions between treatment groups and their respective control groups. Statistical significance of the differences was assumed when $p \leq 0.05$.

A. Life Table Method Using Product-limit Estimation

Diesel Particles - None of the three dose groups had statistically different survival distributions than the distribution of their control group. Mantel-Cox p values were 0.78, 0.31, and 0.31 for low, medium and high dose vs control.

Diesel Particles + Ferric Oxide - None of the three dose groups had statistically different survival distributions than the distribution of their control group. Mantel-Cox p values were 0.41, 0.89, and 0.30 for low, medium, and high dose vs control.

Diesel Extract ± Ferric Oxide - None of the three dose groups had statistically different survival distributions than the distribution of their control group. Mantel-Cox p values were 0.56, 0.81, and 0.98 for low, medium and high dose vs control.

Coke Oven Extract ± Ferric Oxide - None of the three dose groups had statistically different survivial distributions than the distribution of their control group. Mantel-Cox p values were 0.71, 0.62, and 0.73 for low, medium, and high dose vs control.

Cigarette Smoke Condensate ± Ferric Oxide - None of the three dose groups had statistically different survival distributions than the distribution of their control group. Mantel-Cox p values were 0.31, 0.35, and 0.97 for low, medium, and high dose vs control.

Roofing Tar Extract ± Ferric Oxide - None of the three dose groups had statistically different survival distributions than the distribution of their control group. Mantel-Cox p values were 0.56, 0.81, and 0.98 for low, medium, and high dose vs control.

B. Cox Regression Method

A Cox Regression Model was fit using outcome (dead, alive) as the dependent variable and replication, dose, compound, and dose x compound as the independent variables in comparing the various treatments and the controls. The Cox Regression Model was significant in relating the independent variables to the dependent variable outcome ($X^2_{(11)}=72.27$, $p=0.001$). Of the independent variables, replication had the largest effect ($X^2=53.72$, $p=0.0001$). The dose effect as well as the dose and compound interactions were not significant.

The Cox Regression Model was also used to compare the solvent plus ferric oxide control groups. The model was fit using outcome as the dependent variable and replication and compounds as the independent variables. The model, in general, was not significant ($X^2_{(5)}=6.94$, $p=0.26$) in relating the independent variables to the dependent variable outcome. Of the independent variables, no significant effect of the compound was found but the replication effect was significant ($X^2=6.02$, p=0.014).

ORGAN WEIGHTS

The mean organ weights of hamsters for each test article and dose obtained at terminal sacrifice in the first replicate are shown in Table 9. Marked variations in organ weights were due in part to the small sample size and to the pathologic changes seen in the liver and testes. Multiple fluid filled cysts of varying size were present in the liver of many hamsters at necropsy. The cysts increased the weight of the livers especially in the 5.0 mg diesel extract and roofing tar extract treatment groups and the solvent controls of the cigarette smoke condensate group. The weight variation in the testes was due to the presence of small testes in some of the hamsters. The changes in liver and testes occurred with similar frequency among the treated and control hamsters, and therefore were not considered to be treatment-related.

The mean organ weights for hamsters at terminal sacrifice for the second replicate experiment are shown in Table 10. Analysis of variance of these mean organ weights showed that the differences between the test and the control groups were not statistically significant.

PATHOLOGY

Gross and microscopic pathology findings for hamsters that died spontaneously, that were sacrificed in a moribund state, or sacrificed at the termination of the experiment are presented in the following section. Summaries of the gross and microscopic pathology found in hamsters at the scheduled twelve month sacrifices are presented in Appendix E.

Gross Observations

A summary of group incidences of selected gross observations for hamsters in the first and second replicate experiments are shown in Tables 11 and 12. The detailed comprehensive description of gross observations is presented in Appendix B. With a few exceptions, the gross lesions observed in the two replicate studies were similar. Therefore, they are discussed without reference to replicate.

Table 9
Mean Organ Weight at Each Dosage Level
First Replicate (Terminal Sacrifice)

Treatment Group	Dose (mg/wk)	Body Weight (grams)	Organ Weight (grams)					
			Brain	Spleen	Heart	Liver	Kidney	Testes
Diesel Particle	5.0	147	1.16	0.19	0.83	6.24	1.74	2.38
	2.5	141	1.21	0.23	0.83	7.74	1.95	2.25
	1.25	135	1.21	0.22	0.75	6.30	1.70	2.27
Solvent	0.0	156	1.20	0.34	0.83	6.92	1.90	2.88
Diesel Particle + Ferric Oxide	5.0	122	1.18	0.28	0.79	5.42	1.69	1.32
	2.5	128	1.21	0.34	1.04	7.27	2.15	0.96
	1.25	154	1.17	0.25	0.80	6.77	1.75	2.20
Fe O + Solvent	5.0	162	1.24	0.38	0.72	7.99	1.54	2.90
Diesel Extract + Ferric Oxide	5.0	156	1.25	0.21	0.87	11.87	1.87	2.64
	2.5	143	1.21	0.23	0.84	5.44	1.57	2.57
	1.25	134	1.15	0.19	0.97	8.53	1.42	2.35
Fe O + Solvent	5.0	154	1.23	0.18	1.14	6.66	1.73	1.83
Coke Oven + Ferric Oxide	5.0	125	1.12	0.20	0.68	5.29	1.56	2.00
	2.5	150	1.19	0.23	0.84	5.88	1.77	2.40
	1.25	145	1.17	0.21	0.75	5.43	1.54	2.39
Fe O + Solvent	5.0	128	1.18	0.10	1.10	4.69	1.35	2.66
Cigarette Smoke + Ferric Oxide	5.0	161	1.16	0.19	0.84	4.63	3.88	2.70
	2.5	147	1.22	0.27	0.83	6.25	1.71	2.53
	1.25	141	1.11	0.27	0.75	5.52	2.28	2.74
Fe O + Solvent	5.0	165	1.21	0.25	1.02	25.39	2.34	1.22
Roofing Tar + Ferric Oxide	5.0	143	1.20	0.34	0.81	8.99	2.53	2.17
	2.5	160	1.17	0.20	0.87	6.27	1.38	2.30
	1.25	146	1.20	0.28	0.82	6.10	1.83	2.50
Fe O + Solvent	5.0	162	1.14	0.30	0.84	7.48	1.67	2.68
Benzo(a)pyrene + Ferric Oxide	2.0	134	1.15	0.23	0.74	5.27	1.47	1.93
Colony Control	----	145	1.16	0.23	0.80	6.15	1.61	2.10

Table 10
Mean Organ Weight at Each Dosage Level
Second Replicate (Terminal Sacrifice)

Treatment Group	Dose (mg/wk)	Body Weight (grams)	Organ Weight (grams)					
			Brain	Spleen	Heart	Liver	Kidney	Testes
Diesel Particle	5.0	142	1.16	0.23	0.79	5.92	1.89	2.89
	2.5	140	1.16	0.25	0.73	6.55	1.68	2.45
	1.25	145	1.18	0.21	0.86	4.93	1.70	2.65
Solvent	0.0	158	1.18	0.27	0.89	6.53	3.04	2.32
Diesel Particle + Ferric Oxide	5.0	168	1.18	0.23	0.84	7.85	1.86	2.02
	2.5	138	1.17	0.24	0.84	5.69	1.73	2.32
	1.25	143	1.16	0.21	0.84	6.07	1.81	2.90
Fe O + Solvent	5.0	145	1.15	0.24	0.76	7.40	1.49	2.48
Diesel Extract + Ferric Oxide	5.0	146	1.17	0.24	0.72	5.47	1.50	2.81
	2.5	161	1.19	0.25	0.84	6.31	1.74	2.96
	1.25	152	1.19	0.32	0.78	7.84	1.78	2.55
Fe O + Solvent	5.0	152	1.19	0.23	0.75	5.77	1.64	2.70
Coke Oven + Ferric Oxide	5.0	146	1.19	0.20	0.73	6.61	1.53	2.45
	2.5	134	1.13	0.21	0.72	5.60	1.73	2.72
	1.25	159	1.18	0.33	0.80	7.16	1.85	3.00
Fe O + Solvent	5.0	148	1.15	0.28	0.71	6.00	2.00	2.89
Cigarette Smoke + Ferric Oxide	5.0	162	1.25	0.33	0.87	7.52	1.94	2.61
	2.5	140	1.18	0.20	0.83	6.35	1.68	2.31
	1.25	147	1.13	0.27	0.79	5.89	1.62	2.43
Fe O + Solvent	5.0	141	1.17	0.23	0.84	6.28	1.76	2.98
Roofing Tar + Ferric Oxide	5.0	152	1.16	0.22	0.84	7.32	1.70	2.70
	2.5	142	1.20	0.24	0.81	6.09	1.78	2.40
	1.25	170	1.15	0.18	0.84	6.86	1.75	2.41
Fe O + Solvent	5.0	145	1.21	0.30	0.87	7.36	1.73	2.66
Benzo(a)pyrene + Ferric Oxide	2.0	135	1.14	0.22	0.79	6.33	1.72	2.54
Gelatin Saline	0.5%	163	1.16	0.22	0.77	6.73	1.68	2.44
Colony Control	----	150	1.16	0.29	0.78	7.16	1.74	1.50

Table 11

SUMMARY OF GROUP INCIDENCES OF SELECTED GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe₂O₃ 5 mg	DP:Fe₂O₃ 2.5 mg	DP:Fe₂O₃ 1.25 mg	Solvent + Fe₂O₃, 5 mg	DE:Fe₂O₃ 5 mg	DE:Fe₂O₃ 2.5 mg	DE:Fe₂O₃ 1.25 mg	Solvent + Fe₂O₃, 5 mg	COE:Fe₂O₃ 5 mg	COE:Fe₂O₃ 2.5 mg	COE:Fe₂O₃ 1.25 mg	Solvent + Fe₂O₃, 5 mg	CSC:Fe₂O₃ 5 mg	CSC:Fe₂O₃ 2.5 mg	CSC:Fe₂O₃ 1.25 mg	Solvent + Fe₂O₃, 5 mg	RTE:Fe₂O₃ 5 mg	RTE:Fe₂O₃ 2.5 mg	RTE:Fe₂O₃ 1.25 mg	Solvent + Fe₂O₃, 5 mg	BP:Fe₂O₃ 2 mg	Gelatin Saline 0.00
SKIN/SUBCUTIS																										
Edema, diffuse/focal	6/99	----	4/49	4/49	3/49	6/50	3/50	4/48	2/24	6/25	3/49	7/48	----	----	2/48	6/49	3/26	6/49	3/47	----	----	2/48	6/49	2/49	----	3/49	
Abscess	15/99	3/49	9/49	9/49	10/49	7/50	10/50	4/48	1/24	4/49	11/49	4/48	5/25	6/49	9/48	10/49	6/26	16/49	10/47	11/48	----	3/48	9/49	5/49	1/25	10/49	
HEART (AURICLES)																											
Enlarged	17/99	6/50	6/49	8/49	4/49	11/50	6/50	9/49	4/24	6/48	7/49	9/48	3/25	9/48	10/49	6/49	4/25	5/49	7/48	3/47	5/24	5/48	8/49	8/49	4/25	6/49	
TRACHEA																											
Contained black material	----	19/50	15/49	5/49	----	22/50	11/50	10/49	----	----	----	----	1/25	3/47	1/48	----	1/26	1/49	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	
LUNGS																											
Mottled brown	5/99	3/50	3/49	1/49	----	----	----	1/49	4/24	4/48	6/49	3/48	4/25	15/48	19/49	5/49	6/26	4/49	5/48	5/47	5/26	5/48	10/49	2/49	3/25	2/49	
Mottled black	3/99	50/50	43/49	45/49	3/49	48/50	41/50	36/49	5/24	10/48	8/49	5/48	10/25	11/48	15/49	13/48	7/26	15/49	5/48	12/47	6/26	17/48	6/49	5/49	9/25	9/49	
Mottled red	51/99	6/50	16/49	25/49	25/49	11/50	15/50	19/49	12/24	26/48	30/49	30/48	11/25	21/48	25/49	28/49	11/26	33/49	25/48	25/47	18/26	21/48	22/49	17/49	16/25	26/49	
Mottled grey	1/99	2/50	1/49	----	----	----	----	----	----	----	----	2/48	----	----	----	----	----	1/49	2/48	1/47	----	----	----	----	----	5/49	
Nodule	----	----	----	----	----	2/50	1/50	1/49	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	1/49	----	----	1/49	----	----	----	----	2/49	----	1/49	1/48	----	----	----	----	----	1/25	----	
LARYNX																											
Mottled black/contained black material	----	2/50	----	----	----	1/50	1/50	1/49	----	----	----	----	1/25	----	----	----	----	1/49	----	----	----	----	----	----	----	----	
LIVER																											
Cyst	17/98	14/50	9/47	10/49	8/49	12/50	13/50	13/48	5/24	11/48	7/49	9/48	7/25	6/48	8/49	9/49	2/26	10/49	8/47	3/48	8/26	10/47	9/49	8/49	5/26	8/49	
Tan, diffuse/focal/multifocal	2/98	1/50	1/47	4/49	3/49	2/50	2/50	1/48	2/24	2/48	1/49	2/48	1/25	----	4/49	2/49	1/26	2/49	2/47	3/48	3/26	2/47	----	4/49	----	2/49	
Pitted/granular	5/98	----	2/47	3/49	2/49	5/50	2/50	2/48	2/24	1/48	3/49	1/48	----	2/48	4/49	3/49	2/26	2/49	1/47	6/48	1/26	1/47	1/49	2/49	----	1/49	
Enlarged/thickened	6/98	1/50	5/47	6/49	4/49	1/50	2/50	3/48	1/24	1/48	3/49	5/48	----	----	7/49	3/49	3/26	1/49	2/47	1/48	----	3/47	2/49	6/49	----	1/49	
Nodule	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	1/49	----	----	----	----	----	----	1/26	----	
Mass	1/98	----	----	2/49	1/49	----	----	1/48	----	----	----	----	1/25	----	1/49	----	----	----	----	----	----	----	2/49	----	1/26	----	
SPLEEN																											
Enlarged	9/97	5/49	3/47	5/47	5/48	5/49	6/49	6/48	6/24	4/47	4/49	6/48	1/25	6/48	4/49	8/48	3/26	2/49	3/47	10/48	1/24	5/47	7/46	7/48	3/26	7/47	
KIDNEYS																											
Tan/pale/grey	26/98	11/49	12/47	13/47	9/48	17/50	14/50	14/48	6/24	15/48	9/49	13/48	8/25	15/48	16/48	18/49	6/26	11/49	13/47	9/48	7/26	8/47	11/49	12/49	6/26	7/48	
Pitted/granular	13/98	17/50	11/47	15/47	14/48	15/50	16/50	19/48	8/24	15/48	10/49	13/48	9/25	16/48	19/48	19/49	7/26	14/49	19/47	9/48	8/26	19/47	10/49	16/49	6/26	15/48	
Mass	----	----	----	----	1/48	----	2/50	----	----	----	----	----	----	----	1/48	1/49	----	1/49	3/47	----	2/25	1/47	1/49	----	----	----	
TESTES																											
Small/degenerated	33/97	8/49	20/48	20/47	21/49	18/50	22/50	18/48	10/23	16/48	24/49	16/47	10/26	15/48	21/49	25/49	10/26	25/49	21/46	24/48	9/26	19/47	20/49	19/49	8/26	18/49	
NASAL TURBINATES																											
Mass	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	2/49	----	----	----	----	----	----	----	----	----	----	

Table 11 (concluded)

SUMMARY OF GROUP INCIDENCES OF SELECTED GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe$_2$O$_3$ 5 mg	DP:Fe$_2$O$_3$ 2.5 mg	DP:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	DE:Fe$_2$O$_3$ 5 mg	DE:Fe$_2$O$_3$ 2.5 mg	DE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	COE:Fe$_2$O$_3$ 5 mg	COE:Fe$_2$O$_3$ 2.5 mg	COE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	CSC:Fe$_2$O$_3$ 5 mg	CSC:Fe$_2$O$_3$ 2.5 mg	CSC:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	RTE:Fe$_2$O$_3$ 5 mg	RTE:Fe$_2$O$_3$ 2.5 mg	RTE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	BP:Fe$_2$O$_3$ 2 mg	Gelatin Saline 0.00
ADRENAL GLANDS																											
Tan	27/58	19/49	14/47	19/47	13/48	25/49	17/50	15/48	9/25	18/48	13/49	12/48	9/25	14/48	14/48	13/49	4/24	12/49	8/47	11/48	6/24	13/47	13/49	13/49	2/24	11/48	
Enlarged	9/58	11/49	6/47	7/47	5/48	16/49	6/50	5/48	6/24	7/48	7/49	5/48	1/25	8/48	7/48	6/49	2/24	5/49	3/47	6/48	2/24	8/47	6/49	3/49	---	6/48	

Table 12

SUMMARY OF GROUP INCIDENCES OF SELECTED GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony (Control) 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Saline 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Saline + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Saline + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Saline + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Saline + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Saline + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5
SKIN/SUBCUTIS																											
Edema, diffuse/focal	14/100	6/50	8/50	6/49	7/49	4/50	5/50	8/50	2/25	8/50	13/50	7/50	3/25	4/50	6/50	4/48	3/23	10/48	8/50	8/49	2/24	4/49	5/50	5/47	3/24	11/50	7/50
Abscess	----	2/50	3/50	1/49	----	----	----	1/50	3/25	1/50	----	----	----	2/50	3/50	1/48	----	1/48	1/50	----	----	----	3/50	----	1/24	----	----
HEART (AURICLES)																											
Enlarged	25/100	14/50	10/50	9/49	13/49	11/50	18/50	13/50	7/25	7/50	14/50	8/50	4/25	16/50	17/50	11/48	6/23	10/48	13/50	12/49	8/24	11/49	12/50	17/47	6/24	13/50	12/50
TRACHEA																											
Contained black material	----	30/50	21/50	11/49	----	21/50	24/50	17/50	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
LUNGS																											
Mottled brown	6/100	1/50	3/49	1/49	3/49	1/50	1/50	----	4/25	1/50	1/50	3/50	2/25	12/50	11/50	7/48	2/23	6/48	4/50	2/49	1/24	5/49	6/50	5/47	2/24	3/50	3/50
Mottled black	2/100	46/50	41/50	32/49	3/49	45/50	46/50	40/50	13/25	17/50	10/50	13/50	5/25	15/50	14/50	9/48	3/23	27/48	8/50	6/49	7/24	22/45	6/50	----	9/24	6/50	3/50
Mottled red	60/100	15/50	17/50	24/49	34/49	18/50	21/50	29/50	14/25	39/50	35/50	33/50	16/25	23/50	28/50	34/48	16/23	32/48	16/50	35/49	14/24	33/49	32/50	38/47	16/24	31/50	3/50
Mottled grey	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	1/24	----	----
Nodule	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	3/50	----
Mass	----	----	2/50	1/49	----	----	----	----	----	----	1/50	----	----	1/50	----	1/48	1/23	----	----	----	----	----	----	1/47	----	3/50	----
LARYNX																											
Mottled black/contained black material	----	1/50	----	1/49	----	----	2/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
LIVER																											
Cyst	38/100	13/50	11/50	13/48	13/49	10/50	9/50	11/50	11/25	13/50	16/50	15/50	6/25	10/50	12/50	7/48	7/23	9/48	10/50	10/49	5/24	12/49	11/50	9/47	8/24	15/50	17/50
Tan, diffuse/focal/multifocal	7/100	1/50	2/50	4/48	1/47	----	1/50	2/50	1/25	3/50	2/50	4/50	2/25	2/50	1/50	3/48	1/23	2/48	----	2/49	----	1/49	1/50	2/47	3/24	2/50	1/50
Pitted/granular	2/100	6/50	3/50	3/48	1/49	2/50	3/50	3/50	1/25	5/50	1/50	7/50	1/25	3/50	3/50	1/48	1/23	5/48	2/50	1/49	3/24	1/49	2/50	1/47	3/24	2/50	1/50
Enlarged/thickened	5/100	3/50	2/50	6/48	1/49	1/50	3/50	4/50	2/25	1/50	4/50	2/50	----	5/50	5/50	2/48	----	2/48	----	5/49	1/24	2/49	1/50	2/47	----	5/50	1/50
Nodule	----	1/50	----	----	1/49	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	1/24	1/49	----	----	----	----	----
Mass	----	----	----	----	2/49	----	----	----	----	1/50	1/50	2/50	----	1/50	2/50	1/48	----	1/48	----	----	----	----	----	----	----	----	1/50
SPLEEN																											
Enlarged	10/100	4/50	6/50	3/49	6/49	1/50	4/50	3/50	4/25	4/49	7/49	9/50	5/25	3/49	7/50	3/48	3/23	5/47	3/50	8/49	6/24	6/49	7/49	8/47	1/24	3/50	6/50
KIDNEYS																											
Tan/pale/grey	25/100	13/50	13/50	9/49	9/49	10/50	8/50	13/50	4/25	5/50	15/50	13/50	7/25	10/50	15/50	10/48	8/23	16/47	9/50	16/49	6/24	13/49	13/49	19/47	9/24	13/50	14/50
Pitted/granular	61/100	18/50	10/50	17/49	16/49	13/50	21/50	18/50	6/25	10/50	20/50	12/50	9/25	16/50	21/50	15/48	8/23	21/47	13/50	18/49	10/24	19/49	30/49	17/47	8/24	18/50	19/50
Mass	----	1/50	----	----	2/49	----	1/50	----	1/25	----	1/50	2/50	----	----	1/50	1/48	1/23	----	----	----	----	----	1/49	----	----	----	----
TESTES																											
Small/degenerated	31/100	19/49	18/50	17/49	17/49	17/50	15/50	18/50	10/25	14/49	16/50	15/50	9/25	17/50	18/50	15/48	7/23	16/47	15/50	17/49	6/24	19/50	13/49	14/47	8/24	22/50	11/5C
NASAL TURBINATES																											
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----

Table 12 (concluded)

SUMMARY OF GROUP INCIDENCES OF SELECTED GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CDE:Fe_2O_3 5 mg	CDE:Fe_2O_3 2.5 mg	CDE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
ADRENAL GLANDS																											
Tan	28/100	21/50	21/50	13/49	9/49	15/50	24/50	21/50	7/25	20/50	17/50	15/50	5/25	15/50	19/50	15/48	8/23	21/47	12/50	18/49	7/24	14/49	18/49	15/47	8/24	12/50	13/50
Enlarged	16/100	10/50	8/50	3/49	7/49	4/50	11/50	11/50	5/25	6/50	11/50	8/50	1/25	7/50	13/50	7/48	4/23	6/47	5/50	10/49	3/24	7/49	11/49	6/47	3/24	8/50	3/50

Treatment-related lesions were frequently observed in the respiratory system. Mottled black lungs were present in all treatment groups and in almost all hamsters exposed to diesel particles and diesel particles plus ferric oxide. Mottled black lungs were less frequently seen in hamsters treated with ferric oxide (both test groups and solvent controls). Occasionally, mottled black lungs were also seen in untreated hamsters which served as colony controls, gel-saline controls and diesel particle solvent controls. In these hamsters, the mottled black appearance was attributed to hemorrhage or congestion. Mottled brown lungs were seen in a few of the control hamsters. Mottled red lungs were very frequently seen in all exposure and control groups and their presence was attributed to congestion. Masses were observed in a few hamsters in various treatment groups (Tables 11 and 12).

Black material was frequently present in the trachea of hamsters exposed to diesel particles plus ferric oxide at all dosage levels, and in a few hamsters treated with ferric oxide alone. Microscopic examination also revealed the presence of ferric oxide particles in the solvent plus ferric oxide controls.

A variety of gross lesions were observed in other organs. Those organs which consistently showed the greatest number of lesions were the liver, spleen, kidney, adrenal glands, and testes. The lesions in these organs were seen in both control and treatment groups at all dosage levels and did not appear to be treatment related. A few lesions occurred more frequently in one replicate study than the other. Cystic livers and enlarged auricles, and tan adrenal glands were seen more often in the second replicate study than in the first; small testes and enlarged spleens were seen more often in the first replicate study than in the second. Statistical analysis (ANOVA) of these changes indicated that a significantly greater number of hamsters in the second replicate had enlarged auricles and cystic livers than hamsters in the first replicate study. The lesions were considered to be age related, and the higher incidence was attributed to the increase in average life span of hamsters in the second replicate study.

In summary, the gross lesions were consistent with those expected to be present in the respiratory system due to residual from treatment compounds, or due to effects of aging of the hamsters.

Microscopic Observations

The morphology, distribution, and severity of lesions in the target organs, i.e., lungs, pleura, larynx, trachea, and respiratory lymph nodes of hamsters in both replicate studies were similar. Treatment-related lesions were seen in the lungs, pleura, trachea, larynx, and thoracic lymph nodes of hamsters in the various test groups and at all dose levels examined. In lungs, the lesions included the accumulation of test material free and within macrophages in the smaller airways, granuloma formation, adenomatous hyperplasia with ciliary metaplasia, papillary hyperplasia, squamous metaplasia, and fibrosis. Particle-laden macrophages, inflammatory cells, fibrosis, and proliferation of the lining mesothelial cells was seen in the pleura. Test material free and within macrophages was present in the submucosa of the trachea and larynx. Accumulation of test material in the thoracic lymph nodes was accompanied by lymphoid and reticuloendothelial hyperplasia.

The microscopic lesions that were found in each test group and replicate are described in the following section. A summary of the group incidences of histopathologic findings for high and mid-dose groups is presented as Appendix C.

Diesel Particles

First Replicate - Diesel particles were observed free and within macrophages in the alveoli and bronchioles, and occasionally within the interstitial tissues. Oftentimes the particle-laden macrophages formed aggregates which partially or completely obstructed the alveoli. Lymphocytes and neutrophils were seen among the particle-laden macrophages. The inflammatory infiltrate extended from the alveoli and bronchioles to the adjacent peribronchial tissues. Granulomas with centrally accumulated particles were also seen. Papillary hyperplasia with squamous metaplasia was present in approximately 40% of the lungs examined (19/46). Interstitial fibrosis (21/46) and emphysema (38/46) were also seen in the lungs. However emphysematous lesions were present with equal frequency in lungs in the diesel solvent group (27/42)and in the colony control group (58/95).

Macrophages containing test material, inflammatory cells, fibrosis and mesothelial cell proliferation were observed in the pleura.

Small amounts of test material were present in the submucosa of the trachea and larynx, and in thoracic lymph nodes.

Adenomatous hyperplasia (16/42) and papillary hyperplasia (17/42) were observed in the lungs of hamsters in the solvent controls for the diesel particle group. These lesions had a focal distribution and were mild in severity. Three solvent control hamsters (3/42) had small amounts of brown to black particle-like material within macrophages.

Polyps were seen in the trachea of several hamsters at the 5.0 mg dose level.

Second Replicate - The morphology and distribution of the treatment-related lesions were similar to those seen in the first replicate. The lesions included the accumulation of test material free and within macrophages, granuloma formation, adenomatous hyperplasia with ciliary metaplasia, papillary hyperplasia, squamous metaplasia, and fibrosis in the lung. Accumulation of particle-laden macrophages and inflammatory cells, and the proliferation of the lining mesothelial cells was seen in the pleura. Test material was present in the submucosa of the trachea and larynx and accumulation of particles with the proliferation of lymphoid and reticuloendothelial cells was seen in the thoracic lymph nodes.

Particles were found in the lungs of one hamster in the diesel particle solvent group. Minimal to mild lesions of adenomatous hyperplasia were seen in 17/46 (37%) of the hamsters in the solvent group, and in 34/44 (77%) at the 5.0 mg dose level. Minimal changes were observed in the trachea, larynx, and thoracic lymph nodes of hamsters in the solvent group.

Neoplasms were found in the lungs and pleura of hamsters exposed to the 2.5 mg dose of the diesel particles. Lymphoma was seen in the lung of one hamster, a malignant mesothelioma in the pleura and lung of another hamster, and in the pleura of yet another hamster.

Diesel Particles Plus Ferric Oxide

First Replicate - The lung lesions were morphologically similar to those seen in hamsters exposed to diesel particles only except for a slight increase in incidence and/or severity of adenomatous hyperplasia and a very slight decrease in incidence of squamous metaplasia.

Pleural lesions were also similar except for an increase in the incidence of all lesions except inflammatory reaction. The incidence of the inflammatory reaction was actually lower.

Ferric oxide particles were present in the lungs, pleura, trachea, larynx, and thoracic lymph nodes of hamsters in the solvent plus ferric oxide control group. The particle-caused lesions were similar to those seen in the diesel particle plus ferric oxide group, but the incidence and often the severity of these lesions were significantly lower.

A lymphoma involving the lungs of one hamster and a mesothelioma in the pleura of another hamster was seen. Polyps were present in the tracheas of several hamsters at the 5.0 mg dose level, and one hamster in the solvent control group.

Second Replicate - The morphology and distribution of lesions present in the lungs were similar to those observed in hamsters exposed to diesel particles only except that the incidence of adenomatous hyperplasia decreased, inflammatory reaction and granuloma formation increased, and pleural lesions were seen in a smaller number of hamsters.

A mild to moderate accumulation of particles was present in the trachea of all and in the larynx of most (29/31) hamsters exposed to the 5.0 mg dose of diesel particles plus ferric oxide.

Lesions in the solvent plus ferric oxide control group were similar to those observed in the diesel particle solvent control group except that the inflammation reaction was more severe.

A polyp and malignant metastatsis were observed in the lungs of two hamsters exposed to 5.0 mg. An adenoma was present in the lung of one hamster exposed to 2.5 mg, and a malignant metastasis was found in the lung of a solvent control hamster.

Diesel Extract Plus Ferric Oxide

First Replicate - Black particles were present in the lungs of hamsters at the 5.0 mg and 2.5 mg dose levels. The resulting lesions were similar to those described for the diesel particles and diesel particles plus ferric oxide groups, but the number of hamsters with lesions was significantly lower. This included decreased presence of particles and reduced severity of inflammatory reaction. Adenomatous hyperplasia was most apparent at the 5.0 mg dose level. The incidence of these lesions was dose-related but the severity was similar at the 5.0 mg and 2.5 mg levels.

Lesions in the pleura, trachea, larynx and thoracic lymph nodes were similar to those described for the diesel particle group except the lesions were seen less frequently. The incidence and severity of the lesions in the pleura did not appear to be dose related.

A small amount of ferric oxide particles was seen in the lungs, pleura, trachea, larynx and thoracic lymph nodes of a few hamsters in the solvent control group. With a few exceptions the lesions were similar in incidence and severity to those present in the solvent control group of diesel particle plus ferric oxide.

Neoplastic lesions included a seminoma in the lung and a malignant mesothelioma in the pleura of a hamster at the 5.0 mg dose level; an undifferentiated malignant tumor of the lung and pleura of another hamster at the 5 mg dose level; a mesothelioma of the pleura in a hamster at the 2.5 mg dose level; and a polyp in the trachea of a hamster in the solvent control group.

Second Replicate - The lesions in the lungs and pleura were morphologically similar to those observed in the first replicate study. Very few particles were present in the trachea and larynx of a small number of hamsters at the 5.0 mg dose level.

The lung, pleural, tracheal, and laryngeal lesions observed in the solvent control hamsters were similar in severity to those seen at the 5.0 mg and 2.5 mg dose levels except that the incidence was slightly less.

Neoplasms observed in the lungs included an adenoma in one hamster at the 5.0 mg dose level, and an undifferentiated malignant tumor in a hamster at the 2.5 mg dose level. The latter neoplasia also involved the pleura.

Coke Oven Extract Plus Ferric Oxide

First Replicate - The test material in the lungs of hamsters in this group had a slightly different appearance than that of the other groups. The material was brown to black with a yellowish circular component. The morphology of the lesions in the lungs and pleura was similar to that observed in diesel particle groups. However, the incidence of these lesions, especially inflammatory reaction and adenomatous hyperplasia, was generally lower. Similar lesions were observed in the solvent control hamsters with lower incidence and severity.

A few particles were found in the submucosa of the trachea and larynx.

A malignant adenocanthoma and a polyp were seen in the lungs and trachea of two hamsters at the 5.0 mg dose level. A lymphoma was observed in the lungs of a hamster in the solvent control group.

__Second Replicate__ - The test material present in the lungs and the morphology of the lesions were similar to that described for the first replicate experiment. The incidence and severity of the lesions more closely resembled those of the diesel particles plus ferric oxide group but were slightly increased. The pleural lesions were also similar but their incidence was lower.

The incidence and severity of lesions observed in the respiratory organs of solvent control animals was significantly lower than those seen at the 5.0 mg and 2.5 mg dose levels. The exception was the particle accumulation in the trachea and larynx of solvent control hamsters which was greater than that seen at the 5.0 mg dose level.

Carcinomas were observed in the lungs of one hamster at 5.0 mg, one at 2.5 mg, and one in the solvent control group. An adenoma was present in the lungs of a hamster at the 2.5 mg dose level.

__Cigarette Smoke Condensate Plus Ferric Oxide__

__First Replicate__ - The lesions observed in the lung and pleura of these hamsters were similar to those in the diesel particle groups except that the incidence and severity were significantly lower.

A small number of particles were seen in the submucosa of the larynx and trachea. The inflammatory reaction to these particles was mild.

Lesions similar in morphology, incidence, and severity were seen in the solvent control groups.

A lymphoma was present in the lungs, pleura, larynx, and trachea of one hamster and a neoplastic metastasis (sarcoma) in the lung and pleura in another hamster at the 5.0 mg dose level. An adenoma was found in the lungs of one hamster while a polyp was found in the larynx of another hamster in the solvent control group.

Second Replicate - The lesions observed in the lungs and pleura were morphologically similar to those observed in the first replicate experiment.

Adenomatous hyperplasia and the inflammatory responses observed in the lungs and pleura in the solvent group had a slightly greater incidence and basically the same severity as those at the 5.0 mg and 2.5 mg dose levels.

Reticular cell sarcoma was seen in the lung and pleura of one hamster and a polyp involving the larynx of another hamster was found in the solvent control group.

Roofing Tar Extract Plus Ferric Oxide

First Replicate - The incidence and severity of the lesions observed in the lungs and pleura of hamsters were similar to those of the cigarette smoke condensate plus ferric oxide group, except that the incidence of inflammatory reactions and adenomatous hyperplasia was significantly lower at the 2.5 mg dose. Similar lesions were seen in the respiratory organs of hamsters in the solvent control group.

Particles were present in the trachea and larynx in fewer hamsters in this group than in the 5.0 mg cigarette smoke condensate.

Neoplastic lesions seen in the respiratory organs included a lymphoma and reticulosarcoma in the lungs, and a polyp in the trachea at the 5.0 mg dose level; a neoplastic metastasis at the 2.5 mg dose level; and a hemangioma and undifferentiated malignant tumor in the lungs, and polyp in the larynx of two hamsters in the solvent control groups.

Second Replicate - The lesions present in the lungs and pleura were similar in incidence and severity to those observed in the diesel extract plus ferric oxide group. Small amounts of black particles were present in the larynx and trachea.

Ferric oxide particles were observed in the lungs of hamsters in the solvent control group. While the number of hamsters having a reaction to the particles was greater in the solvent control than in the high and mid-dose level, the severity of the lesions was similar.

A polyp attached to the tracheal mucosa was observed in one hamster at the 5.0 mg dose level.

Benzo(a)pyrene Plus Ferric Oxide

First Replicate - Lesions observed in the lungs, pleura, larynx and trachea of hamsters in this group were similar to the diesel particle group except they were less severe and occurred with a lower frequency.

Reticulosarcoma and an undifferentiated malignant tumor were seen in the lungs of two hamsters. Polyps were observed in the larynx and trachea of several other hamsters.

Second Replicate - The morphology, incidence and severity of the lesions observed in the lungs were similar to those observed in hamsters exposed to 5.0 mg diesel extract plus ferric oxide except that adenomatous hyperplasia occurred more frequently in the benzo(a)pyrene group.

Particles were present in the pleura (9/47), trachea (11/39), and larynx (2/39). There was little inflammatory reaction associated with the presence of particles in these organs.

Polyps were seen in 3/48 lungs, 12/39 tracheas, and 3/39 larynx. Carcinomas were present in 5/48 lungs and 4/39 tracheas. Fibroma and sarcoma were found in the tracheas of a few hamsters.

Gelatin Saline

Second Replicate Only - The morphology, incidence, and severity of the lesions observed in the lungs, pleura, trachea, and larynx of hamsters in this group were similar to those observed in hamsters in the diesel particle solvent control group. A few particles were found in the lung of one hamster.

An undifferientated malignant tumor was found in the lung of one hamster.

Colony Control

First Replicate - Adenomatous hyperplasia involving the epithelium lining the terminal and/or respiratory bronchioles was seen in about 26% of hamsters in the colony control group. This change was seen in a significantly lower number of hamsters in the colony control group than the treatment or solvent groups.

Other lung lesions appearing with some frequency in all groups of hamsters regardless of teatment were mononuclear cell infiltrate, congestion, hemorrhage, pneumonia and emphysema.

Significant lesions were not observed outside the respiratory system. All other lesions were generally mild and occurred with the same frequency in all groups of hamsters. Such lesions were regarded as incidental findings ascribed to age, naturally occurring disease or method of sacrifice.

Second Replicate - The lesions observed in the respiratory organs were similar to those seen in the first replicate experiment with the exception that the incidence of adenomatous hyperplasia was sightly lower.

Lymphomas were present in the lungs of one hamster and the lung and pleura of another hamster.

Non-treament related lesions observed in the lungs and other organs of the respiratory system were similar to those observed in the first replicate.

SECTION 7
DISCUSSION

In general, there were no significant differences in the survival rates, organ weights and clinical pathology parameters related to the test compound or test compound concentration within each replicate experiment. However, the survival rates and presence of skin lesions differed significantly between the two replicate trials. These differences were ascribed to the initial housing condition used in the two replicate experiments. In the first replicate the hamsters were housed in groups of three during the first 5 months of experiment and individually thereafter. A considerable degree of fighting was seen among the hamsters during the period of group housing, resulting in skin lesions, severe secondary infections and death. During the second replicate experiment hamsters were group housed for only one month before the individual housing was established.

Hamsters treated with test materials frequently showed significantly lower mean body weights than their respective solvent controls. This effect was usually seen during the 15-week treatment period and in many cases continued during the post-treatment holding period. Inspection of the computer-drawn curves shows that the body weight change difference frequently was caused by a shifting (delay) in weight gain in test material treated hamsters rather than by a reduction in the maximum body weight achieved.

Treatment of hamsters for 15 weeks by once weekly intratracheal instillation of the various test articles induced gross and microscopic lesions of the respiratory tract at response rates which were related to specific test substances. The solvent mixtures which were tested separately also induced responses in the respiratory tract at statistically significant levels (Table 13A). The solvent used for suspending diesel particles (DPSV) induced little pathology in lungs, pleura, larynx or trachea. The only significant responses to instillation of this material were increased papillary hyperplasia and proliferative fibroblasts in the lung and mononuclear cell infiltrates in the trachea. Addition of ferric oxide to this basic solvent mixture (DPFS, DEFS, COFS, CSFS, RTFS) resulted in an increased incidence of a number of

Table 13

Respiratory System Pathology

A. Chi Square Values and Level of Significance for Solvent Control Groups vs Colony Control

	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
LUNGS						
Inflam Reaction	10.86^c	80.36^c	95.25^c	55.37^c	24.43^c	70.16^c
Granuloma	0.46	8.73^b	7.28^b	17.32^c	1.40	1.25
Fibrosis	0.97	4.11^a	1.15	4.11^a	4.26^a	1.45
Hyperplasia Adeno	3.34	9.78^b	11.63^c	6.52^a	5.63^a	4.21^a
Hyperplasia Papil	26.95^c	5.90^a	0.53	2.71	0.44	9.04^b
Metaplasia, Ciliary	0.43	0.92	6.89^b	0.92	0.98	2.65
Metaplasia, Squamous	7.20^b	2.71	0.53	0.45	0.48	2.52
Prolif Fibroblasts	0.97	4.11^a	0.05	0.12	1.67	0.10
PLEURA						
Particles	0.0	47.28^c	31.45^c	34.29^c	33.45^c	13.43^c
Inflam Reaction	0.33	5.83^a	9.08^b	1.66	1.56	1.38
Fibrosis	0.02	0.65	2.59	0.79	0.28	0.02
Proliferation	0.47	0.22	0.29	0.08	1.72	0.16
Mononucle Cell Infil	0.01	1.60	0.53	1.16	0.13	0.20
LARYNX						
Particles	0.47	7.99^b	11.94^c	38.75^c	6.41	47.22^c
TRACHEA						
Particles	0.46	55.05^c	70.20^c	113.1^c	48.48^c	99.12^c
Inflam Reaction	3.63	12.86^c	8.64^b	9.19^b	6.73^b	1.51
Mononucle Cell Infil	7.57^b	28.54^c	6.32^a	19.27^c	7.50^b	10.14^b
THORACIC LYMPH NODE						
Granuloma	0.0	0.0	0.0	0.0	0.0	0.0
Mineralization	0.80	0.46	0.57	0.48	0.45	0.51
MANDIBULAR LYMPH NODE						
Granuloma	0.49	0.24	0.26	0.23	0.16	1.98
Mineralization	0.0	0.0	0.0	0.0	0.0	4.93^a

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[a] $p < 0.05$
[b] $p < 0.01$
[c] $p < 0.001$

Table 13 (concluded)

Respiratory System Pathology

B. Chi Square Values and Level of Significance for High Dose Test Groups vs Solvent Controls[a,b]

	DPOO	DPFO	DEFO	COFO	CSFO	RTFO	BPFO
LUNGS							
Inflam Reaction	95.16[e]	48.27[e]	0.79	29.40[e]	12.76[e]	13.16[e]	0.16
Granuloma	115.5[e]	216.9[e]	103.6[e]	185.8[e]	0.93	18.42[e]	46.77[e]
Fibrosis	25.05[e]	37.28[e]	0.07	48.0[e]	0.93	1.56	1.01
Hyperplasia Adeno	31.38[e]	25.77[e]	0.02	8.96[d]	0.04	0.15	7.93[d]
Hyperplasia Papil	4.14[c]	16.17[e]	12.26[e]	89.71[e]	0.85	2.28	4.32[c]
Metaplasia, Ciliary	19.39[e]	78.87[e]	0.31	27.89[e]	0.01	3.66	16.77[e]
Metaplasia, Squamous	0.26	0.02	2.67	89.96[e]	0.07	1.88	1.60
Prolif Fibroblasts	4.77[c]	11.47[e]	0.02	27.55[e]	0.53	0.0001	2.54
PLEURA							
Particles	120.7[e]	64.09[e]	6.94[d]	33.34[e]	0.98	0.35	2.19
Inflam Reaction	30.72[e]	23.68[e]	0.23	5.02[c]	1.59	3.11	0.67
Fibrosis	87.19[e]	152.3[e]	6.49[c]	67.16[e]	0.08	2.47	13.49[e]
Proliferation	18.47[e]	16.27[e]	9.19[d]	16.69[e]	3.44	0.12	0.16
Mononucle Cell Infil	8.48[d]	4.86[c]	0.02	0.68	3.99[c]	0.06	0.06
LARYNX							
Particles	86.13[e]	134.18[e]	0.52	0.02	0.01	4.06[c]	2.61
TRACHEA							
Particles	165.0[e]	72.73[e]	3.43	0.13	3.52	16.62[e]	9.08[d]
Inflam Reaction	0.32	2.50	2.64	3.34	2.50	0.61	1.80
Mononucle Cell Infil	12.75[e]	5.25[c]	2.58	0.02	0.10	0.07	5.33[c]
THORACIC LYMPH NODE							
Granuloma	0.0	0.0	2.41	2.53	0.0	0.0	94.53[e]
Mineralization	0.0	0.0	0.0	2.53	0.0	0.0	170.1[e]
MANDIBULAR LYMPH NODE							
Granuloma	0.0	0.50	0.44	0.37	0.49	0.41	5.29[c]
Mineralization	0.0	0.50	0.44	0.37	0.49	0.41	8.09[d]

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[a] DPOO compared to DPSV

[b] DPFO, DEFO, COFO, CSFO, RTFO, and BPFO compared to merged ferric oxide + solvent controls

[c] $p < 0.05$

[d] $p < 0.01$

[e] $p < 0.001$

pathologic lesions in hamsters treated with these materials as compared with untreated control animals (CCON).

This baseline data on the effects of treatment with solvent and solvent plus ferric oxide mixtures was required in order to isolate the effects produced by exposure to test materials from those induced by the solvent mixtures in which they were suspended (Table 13B). Diesel emission particles administered alone (DPOO) or in combination with ferric oxide (DPFO) and coke oven emissions (COFO) were the most reactive of the substances tested and produced a variety of pathologic lesions in the respiratory tract at incidence rates significantly higher than their respective controls.

Diesel extract (DEFO) and benzo(a)pyrene (BPFO) induced less respiratory tract pathology than did diesel particles or coke oven emissions but did produce significant pathologic changes. Treatment with BPFO produced granulomas and mineralization in thoracic and mandibular lymph nodes to a significant degree, an effect not seen with other test materials.

Cigarette smoke condensate (CSFO) and roofing tar volatiles (RTFO) induced minimal changes above those produced by the solvent-ferric oxide control treatments. The incidence of respiratory tract lesions induced by these two substances was significantly lower than seen in hamsters treated with the other test materials.

A Chi Square statistic was used to compare paired samples of pathologic effects in order to address particular questions of interest. Three such analyses are shown in Table 14 and relate to the following.

(1) Is the observed pathology due to the total particle load to the respiratory tract or is it reflective of specific reactivity of test materials?

(2) Do the induced pathologic changes show a dose response relationship?

(3) What effect is produced by the addition of an equal quantity of ferric oxide to a reactive test material? That is, does ferric oxide modify the inherent reactivity of the test materials or can it be considered an inert carrier?

The data in Table 14 show that:

(1) Diesel particles alone at a dose level of 5 mg per week induce significantly more pathology than does a 5 mg per week treatment consisting of 2.5 mg of diesel particles admixed with 2.5 mg of ferric oxide. That is, it is the specific properties of diesel particles rather than the total particle load that is significant.

(2) A consistent dose response relationship is seen when the effects produced by 5.0 mg per week treatments with diesel particles are compared to those induced by 2.5 mg per week exposures.

(3) The addition of an equal quantity of ferric oxide to the 2.5 mg dose of diesel particles generally increased the response rates to a modest degree but statistically significant changes were only seen for one class of lesions. That is, in the case of diesel particles admixed with ferric oxide the induced pathology can be attributed to the diesel particles rather than to an experimentally produced dose particle.

Table 14

Comparison of Pathological Effects of Diesel Particle (DPOO) and Diesel Particle Plus Ferric Oxide (DPFO) Test Materials

Lesions	Treatment				Treatment			
	DPOO - 5 mg		DPFO - 2.5 mg		DPOO - 2.5 mg		DPFO - 2.5 mg	
	Pres	ABS	Pres	ABS	Pres	ABS	Pres	ABS
LUNGS								
Inflam. Reaction	76	14	55	39[a]	47	43[a]	55	39
Granuloma	71	19	40	54[a]	23	67[a]	40	54[b]
Fibrosis	29	61	14	80[a]	8	82[a]	14	80
Hyperplasia, Adem.	71	19	54	40[a]	42	48[a]	54	40
Hyperplasia, Papil.	27	63	7	87[a]	4	86[a]	7	87
Metaplasia, Cil.	38	52	6	88[a]	8	82[a]	6	88
Metaplasia, Squa.	8	82	4	90	1	89[a]	4	90
Proliferation, Fibro.	11	79	7	87	3	87[a]	7	87
PLEURA								
Inflam. Reaction	33	51	10	81[a]	7	78[a]	10	81
Fibrosis	62	22	27	64[a]	21	64[a]	27	64
Proliferation	40	44	38	53	28	57[a]	38	53
Mononucl. Cell Infiltrate	14	70	4	87[a]	5	80[a]	4	87

[a] Significantly different from DPOO 5 mg.

[b] Significantly different from DPOO 2.5 mg.

APPENDICES A THROUGH G

LIST OF ABBREVIATIONS

DP -- diesel particles
DE -- diesel extract
COE -- coke oven extract
CSC -- cigarette smoke condensate
RTE -- roofing tar extract
DPFO -- diesel particles plus ferric oxide
DEFO -- diesel extract plus ferric oxide
CSFO -- cigarette smoke condensate plus ferric oxide
COFO -- coke oven extract plus ferric oxide
RTFO -- roofing tar extract plus ferric oxide
BP -- benzo(a)pyrene
BPFO -- benzo(a)pyrene plus ferric oxide
DPOO -- diesel particles alone
DPSV -- diesel particle solvent
DPFS -- diesel particle plus ferric oxide solvent
DEFS -- diesel extract plus ferric oxide solvent
COFS -- coke oven plus ferric oxide solvent
CSFS -- cigarette smoke plus ferric oxide solvent
RTFS -- roofing tar plus ferric oxide solvent
CCON -- colony control
N -- within normal limits
L -- lesions present
M -- tissue not available
I -- tissue inadequate
P -- lesion present, no grade
LN -- lymph node
SG -- salivary gland

APPENDIX A

PREPARATION METHODOLOGY MANUAL FOR BIOASSAY TEST EMULSIONS AND SUSPENSIONS ON IITRI PROJECTS L6119 AND L6138

PREPARATION METHODOLOGY MANUAL
FOR
BIOASSAY TEST EMULSIONS AND SUSPENSIONS
ON
IITRI PROJECTS L6119 AND L6138

CAUTIONS

The various test materials involved in this experiment are being studied for their carcinogenic potential. Therefore, precautions should be taken to protect the laboratory workers as well as the environment from contamination by the test materials.

PERSONAL PROTECTION

1. Materials should be handled and mixed in an operating exhaust hood.
2. Disposable, surgical gloves should be worn by mixing and raw materials handling personnel.
3. Rubber gloves should be worn by glassware washing personnel.
4. NO FOOD or BEVERAGES should be consumed in the work area.

ENVIRONMENT PROTECTION

1. Hood exhaust air should be filtered.
2. Contaminated mixing and collection vessels and the probe generators should be rinsed with solvent and the contaminated solvent should be captured in a waste disposal container stored in the hood for later disposal as a toxic substance.
3. Contaminated gloves, paper towels, disposable bottles, foil weighing pans, etc. should be sealed in plastic bags and disposed of as toxic substances.

The Polytron® mixer is a high energy mixing device that should be used with care. The mixer MUST NEVER BE OPERATED WITHOUT THE PROBE IMMERSED IN A LIQUID. The Polytron® instruction manual is attached and should be read before any attempt is made to operate this mixer.

FOREWORD

This methodologies manual contains instructions for preparing all materials being tested under EPA Grant No. R806929-01-0, "Respiratory Carcinogenesis of Diesel Fuel Emissions" (IITRI Project Nos. L6109 and L6119). It is presumed that users of this manual have some, but limited, knowledge of scientific equipment, terminologies and laboratory procedures. Therefore, definitions of terms used in preparation procedures as well as illustrations of equipment used are provided.

The materials being prepared for testing are:

- diesel (exhaust) particles -- alone in suspension, and with Fe_2O_3 in suspension
- diesel (exhaust) extract -- emulsion, with Fe_2O_3 in suspension
- cigarette smoke condensate -- emulsion, with Fe_2O_3 in suspension
- coke oven extract -- emulsion, with Fe_2O_3 in suspension
- roofing tar (asphalt) extract -- emulsion, with Fe_2O_3 in suspension
- benzo(a)pyrene -- Fe_2O_3 - dry powder
- controls -- vehicle alone and vehicle plus Fe_2O_3

The vehicle for each suspension and emulsion is a mixture of saline, propylene glycol, gum arabic and gelatin.

The administration of materials to animals is being conducted over two, fifteen-week periods--June-September 1980 and October 1980-January 1981.

While the various methodologies described for preparation of materials are generally applicable to preparation of these same materials for any project requirements, the methodology manual as a whole is designed to provide a detailed outline of the materials preparation activities for the chronic testing phase of the L6119 program. Therefore, the materials preparation schedules, personnel listings and identifications of materials being used are specific to the experiments being conducted from June 1980 through January 1981 under L6119.

The contents of this methodologies manual are listed on the following page. The pages containing the precise, step-by-step preparation procedures for each of the materials used in the program are marked by tabs for easier location.

Successful completion of the chronic testing experiment conducted under this EPA grant requires close cooperation and communication between materials preparation personnel (Fine Particles Section of Chemistry Division personnel) and materials user personnel (Life Sciences Division personnel).

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PERSONNEL

MATERIALS PREPARATION

Glassware, vehicle, Fe_2O_3 prep. - primary responsibility

Ken Brown	office - CRB 3B2-2; ext. 4244 lab - CRB 3F3-1,2; ext. 4274 home phone - 422-5697

Glassware prep. - back-up

Elaine Segers	office - CRB 3E2-1; ext. 4245 lab - CRB 3A1-2; ext. 4245 home phone - 463-3491

Emulsion, suspension prep. - primary responsibility

Jean Graf	office - CRB 3A2-1; ext. 4286 lab - CRB 3A1-4; ext. 4286 home phone - 763-1516

Emulsion, suspension prep. - back-up

Elaine Segers	as above

Benzo(a)pyrene and Fe_2O_3 prep. - primary responsibility

Jean Graf	as above

Benzo(a)pyrene and Fe_2O_3 prep. - back-up

George Yamate	office - CRB 3E2-2; ext. 4295 lab - CRB 3C1-1; ext. 4295 home phone - 478-7670

MATERIALS USERS

Primary Contact

Lawrence Dooley	office - MER 2A8-1; ext. 4882 lab - ext. 4882 home phone - 221-7506

Administrative Contact

Alan Shefner	office - CRB 1A9-1; ext. 4852 home phone - 324-4674

LABORATORY FACILITIES

MATERIALS PREPARATION

Raw materials storage	- freezer no. 4, CRB 1E5-2; 3rd shelf from top (extracts and diesel particle "stock" containers)
	- refrigerator freezer in CRB 3F1-1,2 for: benzo(a)pyrene; "working" solutions of extracts
	- general laboratory space, CRB 3F1-1,2 for: vehicle materials; Fe_2O_3
Glassware prep.	- CRB 3F1-1,2 - wash-up CRB 1A1-3 - autoclave (no. 3) CRB Basement - back-up autoclave (no. 4)
Dry powder weighings	- CRB 3F1-1,2 (Torsion balance)
Extract solvent removal	- CRB 3F1-1,2 (hood no. 98)
Extract weighings	- CRB 3A2-2 (Mettler Analytical Balance)
Primary mixing	- CRB 3F1-1,2 (Polytron® homogenizer) in hood no. 97

MATERIALS DELIVERY

Primary delivery point	- MER 2A8-3
Secondary delivery point	- CRB 1A9-1 (Alan Shefner)

GLOSSARY OF TERMS

emulsion - a mixture of two or more liquids in which one liquid is present as finely dispersed droplets throughout the other liquid; the extracts and condensates are emulsified in saline.

suspension - a solid-liquid mixture in which the solid is present as very fine particles dispersed (suspended) in the liquid; the diesel particles are suspended in saline.

vehicle - the liquid in which the second liquid as droplets (in the case of emulsions) or the particles (in the case of suspensions) are dispersed; in this experiment, the vehicle is a mixture of saline, propylene glycol, gum arabic and gelatin.

control or solvent control - the vehicle free of the materials being tested; when Fe_2O_3 is used with the test material, the control also contains Fe_2O_3 and is so indicated--i.e., "Fe_2O_3 control".

mixing vessels - the (glass) containers in which the emulsions and suspensions are prepared (see Figure 1).

measuring vessels - the (glass) containers in which liquid used to prepare suspensions and emulsions are measured (see Figure 2).

collection vessels - the containers in which prepared emulsions (glass) and suspensions (1-ounce plastic-linear polyethylene) are delivered (see Figure 3).

Polytron® - the device used to mix the suspensions and emulsions (see Figure 4); termed mixer throughout preparation procedures.

probe generator - the portion of the Polytron® that is inserted in the material being mixed and actually accomplishes the mixing (see Figure 5); three types of probe generators are used: PT-35/4; PT-10ST; PT-20ST.

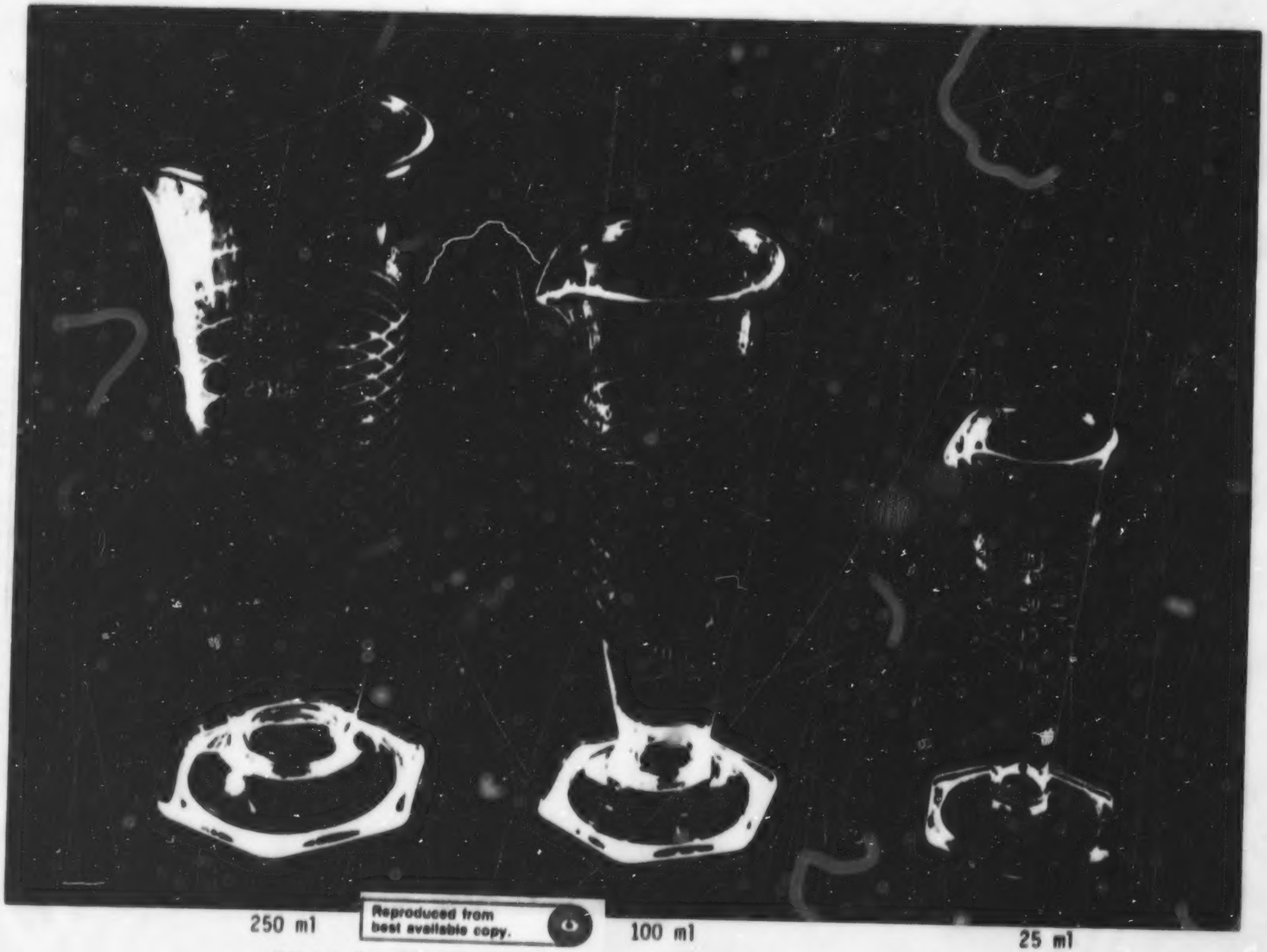
250 ml
100 ml
25 ml

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Figure 1. Mixing vessels = pharmaceutical graduate cylinders.

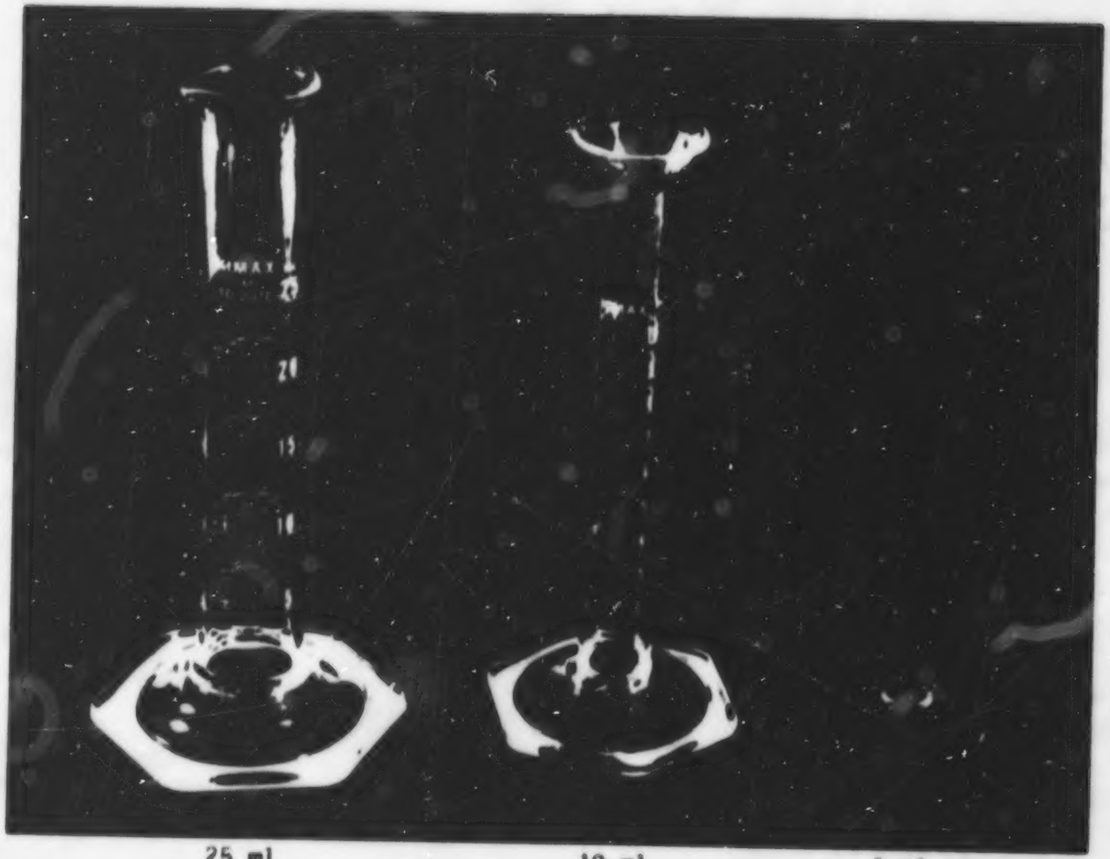
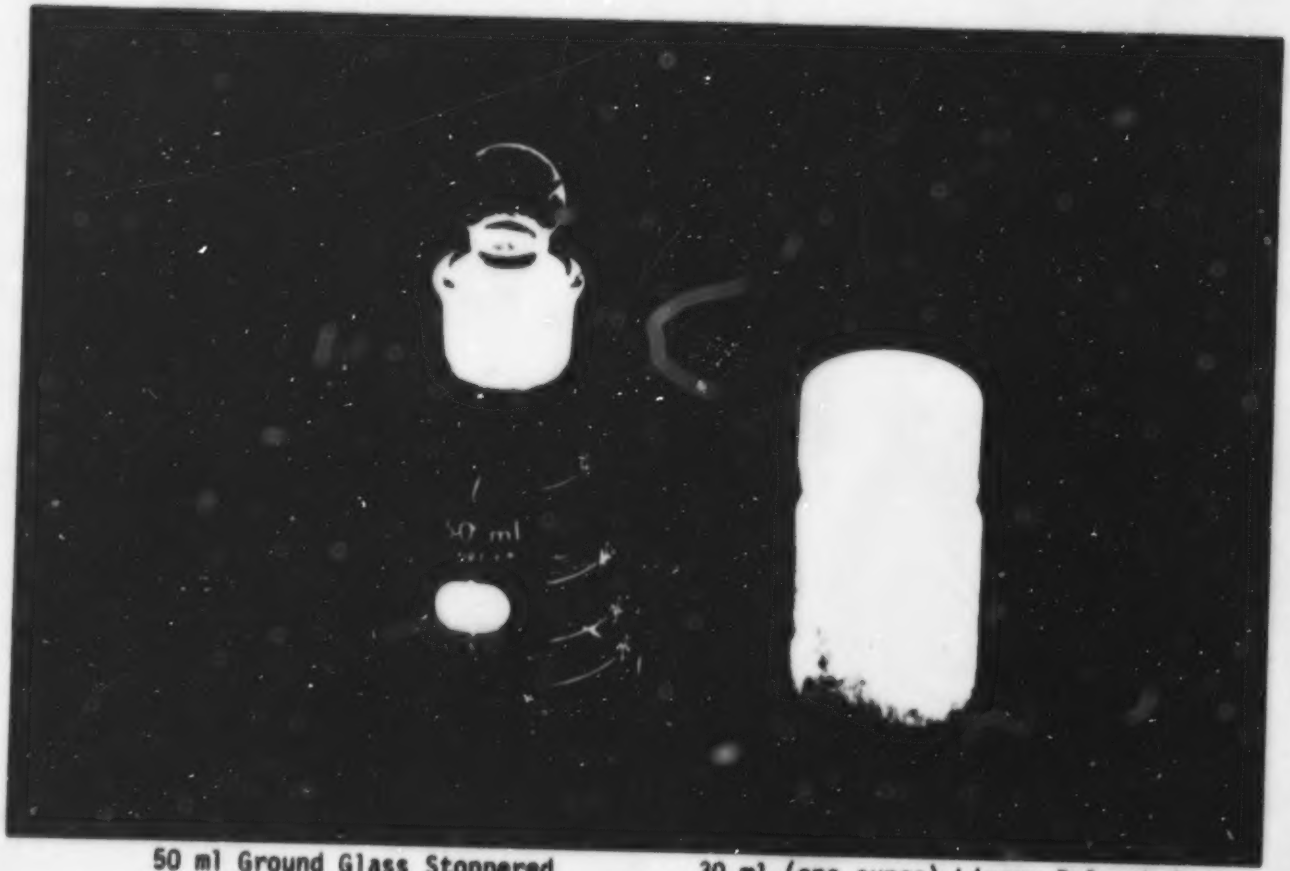

25 ml
10 ml
5 ml

Figure 2. Measuring vessels = graduate cylinders.



50 ml Ground Glass Stoppered
Erlenmeyer Flask -
For Emulsions

30 ml (one ounce) Linear Polyethylene
Plastic Screw-Cap Bottles -
For Suspensions

Figure 3. Collection vessels.

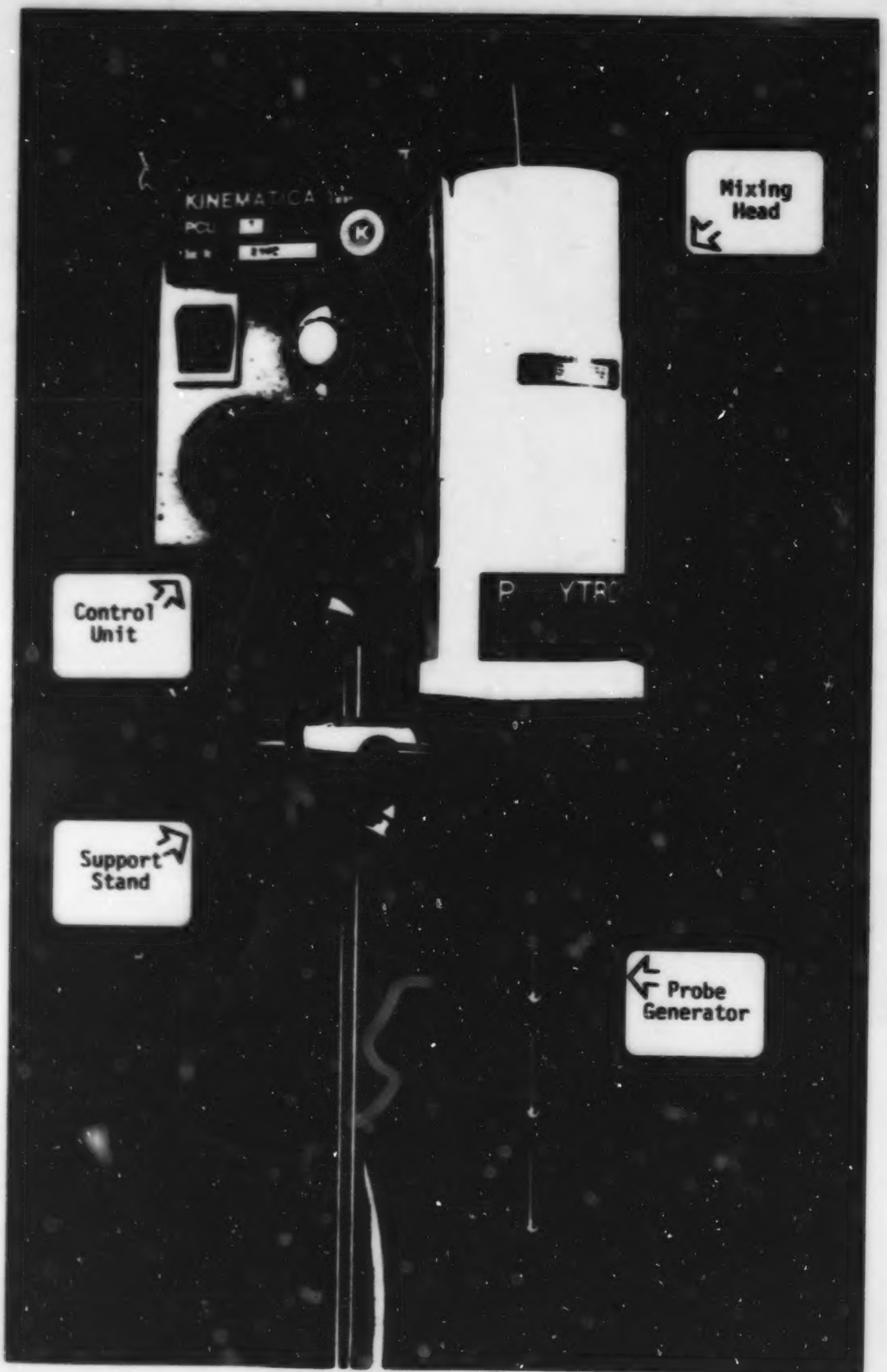

KINEMATICA
PCU
Mixing Head
Control Unit
POLYTRON
Support Stand
Probe Generator

Figure 4. Polytron® mixer.

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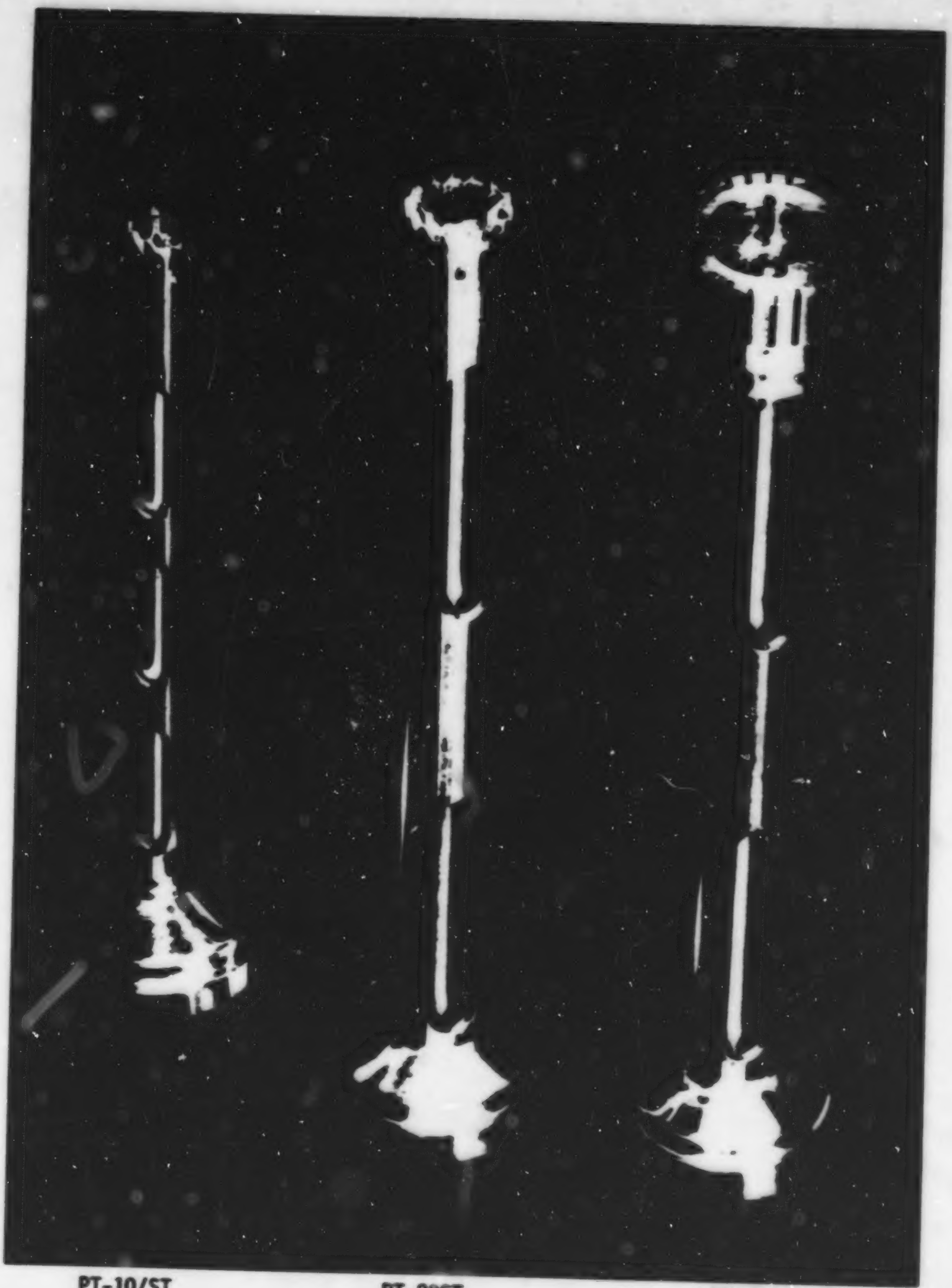

PT-10/ST **PT-20ST** **PT-35/4**

Figure 5. Polytron® probe generators.

MATERIALS PREPARED

Diesel Particle Suspensions (DP)

1.25 mg DP per 0.2 ml
2.5 mg DP per 0.2 ml
5.0 mg DP per 0.2 ml
control = vehicle

Diesel Particle + Fe_2O_3 Suspensions (DP + Fe_2O_3)

1.25 mg DP + 1.25 mg Fe_2O_3 per 0.2 ml
2.5 mg DP + 2.5 mg Fe_2O_3 per 0.2 ml
5.0 mg DP + 5.0 mg Fe_2O_3 per 0.2 ml
control = 5.0 mg Fe_2O_3 per 0.2 ml

Diesel Exhaust Extract + Fe_2O_3 Emulsions (DE + Fe_2O_3)

1.25 mg DE + 1.25 mg Fe_2O_3 per 0.2 ml
2.5 mg DE + 2.5 mg Fe_2O_3 per 0.2 ml
5.0 mg DE + 5.0 mg Fe_2O_3 per 0.2 ml
control = 5.0 mg Fe_2O_3 per 0.2 ml

Cigarette Smoke Condensate + Fe_2O_3 Emulsions (CSC + Fe_2O_3)

1.25 mg CSC + 1.25 mg Fe_2O_3 per 0.2 ml
2.5 mg CSC + 2.5 mg Fe_2O_3 per 0.2 ml
5.0 mg CSC + 5.0 mg Fe_2O_3 per 0.2 ml
control = 5.0 mg Fe_2O_3 per 0.2 ml

Coke Oven Extract + Fe_2O_3 Emulsions (CO + Fe_2O_3)

1.25 mg CO + 1.25 mg Fe_2O_3 per 0.2 ml
2.5 mg CO + 2.5 mg Fe_2O_3 per 0.2 ml
5.0 mg CO + 5.0 mg Fe_2O_3 per 0.2 ml
control = 5.0 mg Fe_2O_3 per 0.2 ml

Roofing Tar (Asphalt) Extract + Fe_2O_3 Emulsions (RTE + Fe_2O_3)

1.25 mg RTE + 1.25 mg Fe_2O_3 per 0.2 ml
2.5 mg RTE + 2.5 mg Fe_2O_3 per 0.2 ml
5.0 mg RTE + 5.0 mg Fe_2O_3 per 0.2 ml
control = 5.0 mg Fe_2O_3 per 0.2 ml

Benzo(a)Pyrene + Fe_2O_3 Powder (BP + Fe_2O_3)

1:1 by mass BP:Fe_2O_3 (supplied as a dry powder)

MATERIALS INSTILLATION SCHEDULE

Phase I begins 2 June 1980
Phase II begins 6 October 1980

MATERIALS	VOLUMES REQUIRED PER WEEK IN ml x NO. OF CONCENTRATIONS			
	MONDAY	TUESDAY	WEDNESDAY	THURSDAY
DP suspensions - 3 concentrations	20 x 3			
Plain solvent	20			
DP + Fe_2O_3 suspensions - 3 concentrations		20 x 3		
Fe_2O_3 control		20		
DE + Fe_2O_3 emulsions - 3 concentrations		20 x 3		
Fe_2O_3 control		20		
CSC + Fe_2O_3 emulsions - 3 concentrations			20 x 3	
Fe_2O_3 control			20	
CO + Fe_2O_3 emulsions - 3 concentrations			20 x 3	
Fe_2O_3 control			20	
RTE + Fe_2O_3 emulsions - 3 concentrations				20 x 3
Fe_2O_3 control				20
BP + Fe_2O_3 powder in suspension				N/A

RAW MATERIALS

Vehicle Components

Saline

- 0.9% Sodium Chloride Irrigation, USP
Travenol Laboratories, Inc.
One Baxter Parkway
Deerfield, Illinois 60015
catalogue no. 2A-71-24
supplied in 1000 ml glass or plastic pour bottles, sterile, nonpyrogenic

Gelatin

- Bacto-Gelatin, lot 556618
Difco Laboratories
Detroit, Michigan
catalogue no. 0143-01
(sufficient supply on hand for entire experiment)

Gum Arabic

- Gum Arabic Powder, USP (fine)
Package Chemical Co.
Boston, Massachusetts
(sufficient supply on hand for entire experiment)

Propylene Glycol

- 1,2 Propanediol, Laboratory Grade, lot 793580-Phase I
1,2 Propanediol, Laboratory Grade, lot 700841-Phase II
Fisher Scientific Co.
Chemical Manufacturing Division
Fair Lawn, New Jersey 07410
catalogue no. P-354

Iron Oxide = Fe_2O_3 (synthetic hematite-roasted copperas red pigment)

- Type R8098R-Pine Indian Red, lot 67
Williams Minerals, Pigments & Metals Division
Pfizer, Inc.
New York, New York 10017
(sufficient supply on hand for entire experiment)

RAW MATERIALS (continued)

Test Materials

1. Diesel Particles - supplied by U.S. EPA from 1978 Olds 350 Diesel Engine
   - Phase I - Run #9490-9492; 9496-9509;9533-9559; 9578
     November 1979; 64.3 g rec'd. 12/5/79
   - Phase II - Run #9533-9559; 9578
     November 1979; 78.8 g rec'd. 12/5/79
2. Diesel Extract - supplied by U.S. EPA from 1978 Olds 350 Diesel Engine
   Run #9490-9588; HWFET; November 1979
   0.0705 g/ml in CH_2Cl_2, 250 ml
   4 x 250 ml rec'd. 12/13/79
   (use one bottle for Phase I; open fresh bottle for Phase II)
3. Cigarette Smoke Condensate - supplied by EPA/ORNL CHEM. REPOSITORS
   Sample No. 6201.164
   25% in acetone (50 g in ~200 ml)
   rec'd. 4/10/79
   (one-half transferred to clean bottle for storage until Phase II begins; one-half in use for Phase I)
4. Coke Oven Extract - supplied by U.S. EPA; only info. on label is: "Contains ~77 g coke oven tar in methylene chloride"
   rec'd. 1/20/80
   (transfer ~20 g to each of two clean glass flasks--one for each phase)
5. Roofing Tar Extract - supplied by U.S. EPA; label indicates: "2nd Asphalt Extract, 200 mg/ml in 100 ml methylene chloride"
   4 x 100 ml rec'd. 5/15/79
   (use one bottle for Phase I; open fresh bottle for Phase II)
6. Benzo(a)Pyrene - 3,4-benzpyrene, 99+%, lot #020897
   Aldrich Chemical Co., gold label
   940 W. Saint Paul Ave.
   Milwaukee, Wisconsin 53233
   catalogue no. 18, 644-9

GLASSWARE, VEHICLE, Fe_2O_3 PREPARATION SCHEDULE (EVERY THREE WEEKS) FOR PARTICLE SUSPENSIONS

	Amount of Material Required	
	FRIDAY (Diesel Particle Suspensions)	MONDAY (Diesel Particle + Fe_2O_3 Suspensions)
AUTOCLAVE:		
100 ml mixing vessel	2	2
250 ml mixing vessel	4	4
10 ml measuring vessel	2	2
plastic collection vessel & cap	15	15
propylene glycol in 150 ml beaker	50 ml	50 ml
saline with:	400 ml	400 ml
gelatin } in 600 ml	2 g	2 g
gum arabic } beaker	1 g	1 g
1 liter bottle of water	1	1
DRY POWDER WEIGHINGS:		
250 mg gum arabic in pan	1	1
0.5 g Fe_2O_3 in pan	0	1
1.0 g Fe_2O_3 in pan	0	1
2.0 g Fe_2O_3 in pan	0	2

NOTE: Extra glassware is always autoclaved in the event some breakage occurs during the preparation procedure.

GLASSWARE, VEHICLE, Fe_2O_3 WEEKLY PREPARATION SCHEDULE FOR EXTRACT EMULSIONS

	Amount of Material Required		
	MONDAY (Diesel Extract Emulsions)	TUESDAY (Cigarette Smoke Condensate + Coke Oven Emulsions)	WEDNESDAY (Roofing Tar Emulsions)
AUTOCLAVE:			
25 ml mixing vessel	5	8	5
100 ml mixing vessel	1	2	1
250 ml mixing vessel	1	2	1
5 ml measuring vessel	2	2	2
25 ml measuring vessel	2	4	2
glass collection vessel & stopper	4	8	4
plastic collection vessel & cap	2	4	2
propylene glycol in 150 ml beaker	50 ml	50 ml	50 ml
saline with:	200 ml	200 ml	200 ml
gelatin } in 400 ml	1.0 g	1.0 g	1.0 g
gum arabic } beaker	0.5 g	0.5 g	0.5 g
1 liter bottle of distilled water	1	1	1
DRY POWDER WEIGHINGS:			
250 mg gum arabic in pan	1	1	1
125 mg Fe_2O_3 in pan	1	2	1
250 mg Fe_2O_3 in pan	1	2	1
500 mg Fe_2O_3 in pan	2	2	2
1.0 g Fe_2O_3 in pan	0	1	0

NOTE: Extra glassware is always autoclaved in the event some breakage occurs during the preparation procedure.

GLASSWARE CLEANING

1. Solvent Rinse

   Rinse used mixing vessels and collection vessels with 10-20 ml reagent grade acetone. Capture rinses in waste container in hood no. 97.

2. Washing

   a. Soak in hot tap water-Alconox solution (follow box directions for soap concentration) overnight; or

   b. Prepare hot tap water-Alconox solution (follow box directions for soap concentration) in large beaker and fill each item to be washed with soap solution.

   c. Scrub with appropriate sized brush to create thick lather.

   d. Pour out lather and rinse under flowing stream of hot tap water until all soap lather is removed.

   e. Inspect washed item to insure that it is clean; scouring powder may be required to remove stubborn stains; Q-Tips may be required to reach crevices; rinse thoroughly under hot tap water if additional washing is performed.

3. Rinsing

   Follow tap water rinse with a rinse of (laboratory) distilled water sprayed from a standard wash bottle.

4. Draining

   Invert on clean paper towels to drain distilled water from cleaned item.

WEIGHING OF DRY POWDERS WITH THE TORSION BALANCE

1. Check the schedule for the day's requirements of weighed dry powders.

   Note: For time efficiency, weigh the gum arabic and gelatin (needed for the vehicle preparation) prior to the glassware and vehicle preparation for autoclaving, and leave the weighing of the iron oxides until after the glassware has been placed in the autoclave.

2. Follow the posted instructions for operation of the Torsion balance.

   Note: If too much material has been placed in the sample pan during the weighing, DISCARD THE EXCESS; DO NOT RETURN EXCESS MATERIAL TO THE STOCK CONTAINER.

3. Upon completion of weighings, cover the weighed samples with aluminum foil and place labels on the samples; check to insure that all stock containers have been completely sealed.

GLASSWARE AND VEHICLE PREPARATION FOR AUTOCLAVING

1. Check the schedule for required glassware (and plastic) items.

2. Cover openings on mixing, measuring and collection vessels with a doubled layer of heavy-duty aluminum foil; foil should extend down the sides of the vessel 0.5 to 1 inch below the vessel opening.

3. Wrap the lids for the collection vessels with heavy-duty aluminum foil (Figures 6 and 7).
   a. For ground glass stoppers, cut a strip of foil that is at least two times the circumference of the stopper and two times its length; wrap the stopper by starting at one end of the foil and rolling the stopper along its circumference; fold the excess length of foil over the ends of the stopper.
   b. For plastic screw caps, cut a strip of foil thats length is 1.5 times the cap diameter and width is two times the cap diameter. Set a cap, open side down, in the center of the foil and fold the (length) ends of the foil up until they meet over the center of the cap; fold the ends over each other and roll the seal made down onto the cap; then fold the (width) ends of the foil over onto the cap.

4. Check the schedule for vehicle requirements.

5. Make the saline-gelatin-gum arabic solution in the required volume (see schedule for the volume of saline and the masses of gelatin and gum arabic).
   a. Measure the saline volume required with a clean, 250 ml pharmaceutical graduate.
   b. Pour the saline into the designated size beaker.
   c. Weigh the gelatin into a foil pan on the Torsion balance.

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Figure 6. Wrapping of ground glass stoppers for autoclaving.

Figure 7. Wrapping of plastic caps for autoclaving.

GLASSWARE AND VEHICLE PREPARATION FOR AUTOCLAVING (continued)

d. Weigh the gum arabic into the same pan with the gelatin.

e. Pour the gelatin-gum arabic from the weighing pan into the measured volume of saline in the beaker.

f. Cover the beaker with a doubled layer of heavy-duty aluminum foil.

6. Pour 50 ml of propylene glycol into a 150 ml beaker (using the beaker markings as the guide for 50 ml); cover with a doubled layer of heavy-duty aluminum foil.

7. Fill a distilled water-rinsed empty saline bottle two-thirds full with distilled water and cover the mouth loosely with a doubled layer of heavy-duty aluminum foil.

8. Place the beakers of saline solution and propylene glycol in a porcelain clad metal pan lined with paper towels; carefully place the other glassware required for the day's preparations in the pan; use a second pan if necessary so that the glassware items are not stacked upon each other; place the bottle of water in a pan (for carrying to the autoclave).

9. Carry the pan(s) to the autoclave.

   Note: Autoclaving must be completed at least two hours prior to the time the items are required for use.

AUTOCLAVING GLASSWARE AND VEHICLE

1. Unload any items from the autoclave that may be present after ascertaining from person responsible that items can be removed.

2. Load the pan(s) into the autoclave.
   a. Place the pan(s) sideways on the rack in the autoclave.
   b. Separate two pans by at least six inches.
   c. Remove the bottle from the pan and set it separately on the autoclave rack at least six inches from the pan(s).

3. Close the autoclave door and seal by rotating the door wheel until it stops.

4. Follow the instructions posted on the autoclave for operating under the following conditions:
   a. automatic cycle (on switch--illuminates orange light)
   b. sterilization cycle timing of 30 minutes
   c. slow exhaust (no drying cycle)
   d. steam sterilization

   Temperature and pressure are preset for the sterilization cycle.

5. Sign the autoclave use log and turn on autoclave.

   Note: For the autoclave in CRB 1A1-3, be sure that the red "steam" light goes on when the cycle knob is rotated to "STER"; if it has not gone on, rotate the knob clockwise a little further until it goes on.

6. Return to remove the pan(s) and bottle from the autoclave 45 to 60 minutes after the unit was turned on.

AUTOCLAVING GLASSWARE AND VEHICLE (continued)

a. Insure that the cycle is complete by observing that the "STERILE" light (blue) is lit (and that the buzzer is sounding).

b. Slowly open the door and allow remaining steam to gradually escape.

7. Remove the bottle with a heat resistant glove and squeeze the foil cover on tightly; place the bottle in the vacant spot left in the pan from which it was removed prior to autoclaving.

8. Remove the pan(s) with gloved hands and return them to the prep. laboratory to cool before use.

9. Check to make sure there was no breakage of items autoclaved.

PREPARATION OF DIESEL PARTICLE SUSPENSIONS

STARTING MATERIALS (see RAW MATERIALS list)

Diesel Particles: appropriate phase material
Vehicle: saline with:
  0.5% wt/vol gelatin
  0.25% wt/vol gum arabic
propylene glycol (added at 10% vol/vol) with
  0.5% wt/vol gum arabic in suspension
Iron Oxide: synthetic hematite

SUSPENSION CONCENTRATIONS

Diesel particles alone as 5, 2.5 and 1.25 mg per 0.2 ml suspensions, prepared individually

Diesel particles + Fe_2O_3, each present in 5, 2.5 and 1.25 mg per 0.2 ml suspensions, prepared individually

Controls - 1 plain solvent, 1 with 5 mg Fe_2O_3 per 0.2 ml

PREPARATION FREQUENCY

Prepared every 3 weeks

Minimum volume required weekly is 20 ml

Minimum mixing volume is 80 ml - yields 70 ml = 3 weeks of material plus laboratory retain sample

DRY POWDER REQUIREMENTS FOR 80 ml MINIMUM VOLUMES

5 mg per 0.2 ml x 80 ml = 2.0 g
2.5 mg per 0.2 ml x 80 ml = 1.0 g
1.25 mg per 0.2 ml x 80 ml = 0.5 g

GLASSWARE, PLASTICWARE REQUIREMENTS (see glassware preparation schedule)

250 ml mixing vessels - 1 per concentration per suspension type
100 ml mixing vessels - 1 per control
10 ml measuring vessels - 1 per suspension type

30 ml plastic collection vessels - 3 per concentration per suspension type and 3 per control type

extra 100 ml, 250 ml mixing vessels for probe cleaning

HARDWARE REQUIREMENTS

Polytron® mixer and control unit

Polytron® PT-35/4 probe generator

Polytron® PT-20ST probe generator (for Fe_2O_3 containing suspensions only)

WEIGHING OF DIESEL PARTICLES

1. Remove "stock" bottle of particles from the low temperature freezer.

2. Pour into a small, wide mouth "working" bottle the estimated volume of particles required for the day's preparations (pouring should be done in the hood in 3F1-1,2).

3. Return the "stock" bottle to the low temperature freezer immediately.

4. Weigh the diesel particles for each concentration in foil weighing pans on the Torsion balance from the small "working" bottle. Weighings should be performed in a hood.

5. Discard excess DP remaining in the "working" bottle.

   Note: Pour excess into labeled bottle that is kept in the refrigerator freezer in CRB 3F1-1,2.

PREPARATION OF SUSPENSIONS FOR MIXING WITH POLYTRON®

1. Pour the diesel particles from the weighing pans into 250 ml mixing vessels; label each vessel and re-cover the vessel with the sterile aluminum foil.

2. Mix the propylene glycol-gum arabic by pouring 250 mg of gum arabic from its weighing pan into the sterilized 50 ml of propylene glycol; swirl to thoroughly mix and suspend the gum arabic.

3. Measure 8 ml of the propylene glycol-gum arabic and add to the mixing vessels containing the diesel particles; re-cover the mixing vessels with the sterile foil.

   Note: Propylene glycol is viscous and will adhere to the measuring vessel walls. Therefore, measure out 9 ml in the measuring vessel and pour from the measuring vessel until the fluid stream stops; do not allow the fluid to continue to drip out. (Upon returning the measuring vessel to its upright position, it will be observed that the fluid adhering to the vessel walls totals 1 ml.)

4. Measure 8 ml of the propylene glycol-gum arabic and pour it into a 100 ml mixing vessel. This is for the CONTROL suspension.

5. Wet the diesel particles with propylene glycol by swirling and tilting the 250 ml mixing vessels.

   Note: The 5 mg per 0.2 ml suspension requires extra care in assuring wetting of the particles. In addition to the swirling and tilting, lay the mixing vessel on its side for 5 minutes and then rotate it to the opposite side and let it lay for another 5 minutes. The swirling and tilting activities should continue until no powder can be shaken loose.

6. Pour the saline vehicle from its beaker into each mixing vessel very SLOWLY. Pour to the (hand-drawn) 80 ml mark on the mixing vessels. Saline vehicle should be added to the control suspension mixing vessel at this time also.

PREPARATION OF DIESEL PARTICLE SUSPENSIONS (continued)

MIXING THE SUSPENSIONS WITH THE POLYTRON®

1. Attach the clean PT-35/4 generator to the mixing unit per instrument instruction manual.

2. Rinse and sterilize the generator.
   a. Thoroughly saturate the probe with 10-20 ml of 100% ethanol (dispensed from a wash bottle) and discard this rinse.
   b. Fill a sterilized 250 ml mixing vessel two-thirds full with the sterile distilled water.
   c. Insert the generator in the sterile water and mix at SPEED 6 for 2-3 minutes.
   d. Wick-off the excess water from the generator by placing the mixing vessel interior walls against the sides of the generator.

3. Mix the diesel particles with the vehicle in the following order according to the times and speeds listed:

   control suspension - 1 to 2 minutes at SPEED 5.5
   1.25 mg/0.2 ml - 2 to 4 minutes at SPEED 5.5
   2.5 mg/0.2 ml - 2 to 4 minutes at SPEED 5.5
   5.0 mg/0.2 ml - 3 to 5 minutes at SPEED 5.5

   Mix by placing the vessel under mixer so that the generator reaches as far into the vessel as possible. Turn the mixer on to the prescribed speed. Mix for 15 to 30 seconds before beginning an up-and-down and side-to-side motion of the mixing vessel. After initial mixing (the 15-30 seconds), begin the motion to insure that all the particles are thoroughly mixed by the generator. Motion is necessary to allow all particles to come in contact with the generator and to minimize formation of a vortex; therefore, change directions of side-to-side motion so as to disrupt any circular flow of suspension that forms because of the spinning rotor inside the generator shaft. When mixing is complete, wick-off as much suspension as possible from the generator with the sides of the mixing vessel and cover the suspension.

Note: Foaming will occur to varying degrees and some heating of the suspension will also occur because of the energy released from collisions of particles with each other. Mixing periods are designed to thoroughly mix particles with only a small, detectable heat rise occurring. If the mixing vessel is actually hot, mixing was for too long a period and the suspension should be discarded. Approximate volumes of fresh-mixed suspensions with foam are:

control - 150 ml
1.25 mg per 0.2 ml - 250 ml
2.5 mg per 0.2 ml - 200 ml
5.0 mg per 0.2 ml - 150-200 ml

4. Rinse the generator with acetone, collecting the rinse in a contaminated solvent storage vessel. (The particle-containing acetone rinse should be treated as a toxic substance.) Rinse the generator with distilled water by mixing in a 250 ml vessel. Remove the generator for soap-and-water cleaning.

5. THE NEXT STEPS ARE DEPENDENT ON THE SUSPENSION TYPES TO BE MADE.

5A. DIESEL PARTICLES ONLY AND SOLVENT CONTROL SUSPENSIONS

a. Allow the foam to reduce before transferring the suspensions to the plastic collection bottles--this should be approximately one hour.

b. Swirl the suspension, remove the foil cover, and pour the suspension into three labeled, sterile plastic bottles. Fill each bottle approximately two-thirds full. Fill the bottles one at a time, removing and replacing the foil covers on each bottle one at a time.

Note: The three bottles of the 5 mg/0.2 ml dose must be filled to near capacity because substantial foam will still be present at the time of pouring.

c. Pour the remaining suspension from the mixing vessel into a suitable, labeled container for the laboratory retain sample.

d. Unwrap the screw caps, one at a time, and place them on the plastic sample bottles in place of the foil covers.

5B. DIESEL PARTICLES PLUS Fe_2O_3 AND Fe_2O_3 SOLVENT CONTROL SUSPENSIONS

a. Install the PT-20ST generator on the Polytron®.

b. Pour the weighed portions of Fe_2O_3 into the appropriate mixing vessels.

c. Sterilize the generator as described previously for the Diesel Particle Mixing steps.

d. Mix the Fe_2O_3 control suspension.

d_1 Place the mixing vessel under the generator so that the generator touches the bottom of the vessel.

d_2 Mix for 2 to 3 minutes at SPEED 6 while moving the vessel around the generator in an up-and-down and side-to-side motion. Begin this motion after the first 15 seconds of mixing.

d_3 Turn off the mixer, remove the vessel from the generator, and wick-off as much suspension as possible from the generator with the walls of the vessel.

d_4 Immediately pour the suspension into labeled plastic bottles, one at a time, re-covering each bottle as it is filled two-thirds full. The remaining suspension to be retained as a laboratory sample should also be poured into a labeled storage container at this point.

Note: It is important to pour each finished suspension into the plastic collection vessels immediately after mixing so that no settling of the iron oxide occurs. The iron oxide prevents significant foaming of the suspensions during mixing and therefore a waiting period before bottling is not required.

d_5 Rinse the generator in a fresh portion of sterile distilled water by mixing at SPEED 6 for 1-2 minutes. Wick-off the excess water before proceeding with the DP-Fe_2O_3 suspensions.

e. Mix the Fe_2O_3 into the diesel particle suspensions by following instructions d_1 through d_4 for the Fe_2O_3 control suspensions. Mix in the following sequence:

1.25 mg per 0.2 ml
2.5 mg per 0.2 ml
5.0 mg per 0.2 ml

Place the screw caps on the bottled suspensions one at a time. Rinse the generator with acetone (to be discarded as a toxic waste), then with distilled water; remove the generator and wash thoroughly with soap and water.

PREPARATION OF DIESEL EXTRACT AND Fe_2O_3 EMULSIONS

STARTING MATERIALS (see RAW MATERIALS list, p. 11 & 12)

Diesel Extract:	appropriate phase material
Vehicle:	saline with: 0.5% wt/vol gelatin 0.25% wt/vol gum arabic propylene glycol (added at 10% vol/vol) with 0.5% wt/vol gum arabic in suspension
Iron Oxide:	synthetic hematite

EMULSION CONCENTRATIONS

Diesel extract and Fe_2O_3, each present in 5, 2.5 and 1.25 mg per 0.2 ml emulsions, prepared individually

Control - 1 with 5 mg Fe_2O_3 per 0.2 ml

PREPARATION SCHEDULE (see glassware preparation schedule, p. 14)

Prepare fresh every week not less than 2 hours nor more than 18 hours before needed--i.e., late Monday

EXTRACT VOLUME REQUIREMENTS FOR WEEKLY EMULSION DELIVERY

5 mg per 0.2 ml x 20 ml = 500 mg = 10 ml of 50 mg/ml working solution

2.5 mg per 0.2 ml x 20 ml = 250 mg = 5 ml of 50 mg/ml working solution

1.25 mg per 0.2 ml x 20 ml = 125 mg = 2.5 ml of 50 mg/ml working solution

GLASSWARE, PLASTICWARE REQUIREMENTS (see glassware preparation schedule)

25 ml mixing vessels - 1 per concentration and for control
5 ml measuring vessels - 1
25 ml measuring vessels - 2
50 ml glass collection vessel - 1 per concentration
30 ml plastic collection vessel - 1 for control
extra 100 ml, 250 ml mixing vessels for probe cleaning

PREPARATION OF DIESEL EXTRACT AND Fe_2O_3 EMULSIONS (continued)

HARDWARE REQUIREMENTS

Polytron® mixer and control unit
Polytron® PT-10ST probe generator
Hot plate with hot water bath
Solvent blow-off apparatus:
    nitrogen cylinder (high purity dry grade)
    single-stage regulator with delivery stream valve
    tubing and tees
    ring stands and four 3-prong clamps
    pasteur pipettes

PREPARATION OF THE "WORKING" SOLUTION FROM THE "STOCK" SOLUTION

1. Remove the appropriate phase "stock" solution bottle (70.5 mg/ml) from the low temperature freezer and allow the solution to come to room temperature.

2. Pipette 71 ml of "stock" solution into a 100 ml volumetric flask.
    a. 1 x 50 ml pipette
    b. 1 x 20 ml pipette
    c. 1 x 1 ml pipette

3. Fill the 100 ml volumetric flask to the indicating mark with methylene chloride to produce a 50 mg/ml "working" solution.

    Note: 100 ml of this solution is sufficient to prepare 5 weeks of emulsions. Additional "working" solutions must be prepared every 5 weeks.

4. Stopper the flask and gently shake to complete the preparation of the "working" solution.

    Note: Carefully loosen and remove the stopper to vent the vapors that have built up from the shaking action.

PREPARATION OF DIESEL EXTRACT AND Fe_2O_3 EMULSIONS (continued)

5. Return the "stock" solution to the low temperature freezer.

6. Label the "working" solution and place it in the refrigerator freezer in CRB 3F1-1,2 until it is needed.

PREPARATION OF GLASSWARE, VEHICLE AND EXTRACT FOR THE EMULSIFICATION

1. Check the schedule for the required glassware, vehicle volume, and weighed iron oxide portions required. Prepare and autoclave glassware and vehicle according to instructions in "Glassware and Vehicle Preparation for Autoclaving" and "Autoclaving Glassware and Vehicle".

2. Fully dry the mixing vessels.
   a. Rinse with ethanol
   b. Dry in the laboratory oven (80°C)
   c. Cool to room temperature in a desiccator
   d. Equilibrate to ambient humidity conditions (30 minutes outside of the desiccator, once cooled)

3. Remove the "working" solution from the refrigerator freezer (CRB 3F1-1,2) and allow it to come to room temperature.

   Note: Methylene chloride expands considerably in volume in going from freezer temperature to room temperature.

4. Label and weigh the mixing vessels on the METTLER analytical balance to the nearest 0.1 mg (see the SOP for this balance); record these weights in the laboratory logbook.

PREPARATION OF DIESEL EXTRACT AND Fe_2O_3 EMULSIONS (continued)

5. Measure out the required volumes of the "working" solution into the mixing vessels with the labeled pipettes kept in hood no. 97.
    a. 2.5 ml - for the 1.25 mg per 0.2 ml
    b. 5 ml - for the 2.5 mg per 0.2 ml
    c. 10 ml - for the 5 mg per 0.2 ml

6. Turn the hot plate on to the MEDIUM setting and place a (large crystallizing) dish of water--two-thirds full--on the hot plate.

7. Blow the solvent off the "working" solution of extract that has been measured into the mixing vessels.
    a. Place each mixing vessel below the nitrogen delivery tubes in the hood (no. 98, CRB 3F1-1,2).
    b. Insert a clean pasteur pipette in the end of each nitrogen delivery tube that is to be used.
    c. Insert the pasteur pipettes into each mixing vessel and adjust the tubing length (by sliding the tubing up or down in the 3-prong holding clamp) so that the pipette is approximately one-quarter inch above the solution surface.
    d. Check the nitrogen cylinder and regulator setting to see if:
        d_1 the tank valve is open
        d_2 there is sufficient nitrogen in the tank (change the tank if empty according to the posted SOP above the cylinder rack)
        d_3 the regulator valve is set to 15-20 psi
    e. Open the delivery stream valve to start the flow of nitrogen.

    Note: Opening this valve will drop the regulator pressure to 10-15 psi, which is satisfactory.

f. Check the delivery of the nitrogen to the mixing vessels.

  f_1 Insure that the flow rate is not too fast to cause splashing and loss of some of the extract solution--raise the pipette if this is the case.

  f_2 The pipette must be checked during the entire course of the blow-down (30 to 45 minutes) so that it can be lowered as the solution level drops.

  Note: A thick layer of extract may develop and prevent the nitrogen stream from removing all the solvent; break this layer by manually moving the nitrogen stream over the surface of the extract, concentrating it near the center, then the sides.

g. The solvent removal is complete when the mixing vessel returns to room temperature (evaporation of the solvent makes the mixing vessel cold).

h. Turn off the nitrogen delivery stream valve and remove the pipettes from the vessels.

8. Return to the METTLER analytical balance and reweigh the mixing vessels which now contain the extract without solvent.

   a. Follow the SOP for using the balance.

   b. Record the vessel + extract weight above the empty vessel weight previously recorded (step 4).

   c. Subtract the empty vessel weight from the vessel + extract weight to yield the weight of the extract.

   Note: The extract weight should be ±10% of the desired weight; if the extract weight is outside of this 10% range, add more extract (remembering to blow-off the new solvent now added) or calculate how much larger the total emulsion volume must be to yield the desired mg per 0.2 ml dose (remembering also to increase the volume of propylene glycol and the weight of the iron oxide that must be added to the emulsion).

9. Pour the measured 250 mg of gum arabic into the sterilized 50 ml of propylene glycol and swirl to form a suspension.

10. Measure 2 ml of propylene glycol-gum arabic (with the 5 ml measuring vessel) into each mixing vessel containing extract and into an empty, sterile 25 ml mixing vessel (for preparation of the control).

    Note: Propylene glycol is viscous and will adhere to the walls of the measuring vessel; therefore, measure out 2.5 ml and pour the propylene glycol out until the fluid stream stops; do not allow the propylene glycol to continue to drip out. Upon returning the measuring vessel to the upright position, it will be observed that 0.5 ml of propylene glycol remains and therefore 2.0 ml was delivered to the mixing vessel.

11. Measure 18 ml of saline vehicle with a 25 ml measuring vessel and pour it into the control suspension mixing vessel.

12. Match-up the mixing vessels, labeled collection vessels, and pans of iron oxide in a line on the lab bench closest to the hood in which the mixer is located (hood no. 97).

    Note: Remove the foil covers from the labeled pans of iron oxide and inspect the contents to insure they contain the quantities indicated on the label--i.e., the 2.5 mg pan contains twice as much as the 1.25 mg pan but only half as much as the 5 mg pan.

PREPARATION OF DIESEL EXTRACT AND Fe_2O_3 EMULSIONS (continued)

MIXING THE DIESEL EXTRACT EMULSIONS AND CONTROL WITH THE POLYTRON®

1. Attach the clean PT-10ST probe generator to the mixing unit (see instrument instruction manual) and sterilize.
    a. Rinse with 10-20 ml 100% ethanol from a wash bottle and discard this rinse.
    b. Fill a sterile spare mixing vessel (100 or 250 ml) two-thirds full with sterile distilled water.
    c. Mix at SPEED 6 for 2-3 minutes.
    d. Wick-off the water with the sides of the mixing vessel.
    e. Re-cover the mixing vessel of sterile water with foil.

2. Mix the control suspension (vehicle only) for 1-2 minutes at SPEED 6.
    a. Add the weighed iron oxide.
    b. Mix 1-2 minutes at SPEED 6.
    c. Wick-off the excess suspension with the sides of the mixing vessel.
    d. Immediately pour the control suspension into a plastic collection vessel and re-cover the collection vessel with foil.

3. Rinse the probe in a fresh portion of sterile water by mixing at SPEED 6 for 1-2 minutes; wick-off the excess water with the sides of the mixing vessel.

4. Mix the extracts, beginning with the 1.25 mg/0.2 ml concentration.
    a. First swirl the mixing vessel to mix the propylene glycol with the liquid, oil-like phase of the DE.

PREPARATION OF DIESEL EXTRACT AND Fe_2O_3 EMULSIONS (continued)

b. Set the mixing vessel in the hot (80°C) water bath to soften the semi-solid tarry phase of the DE; remove from the bath every 30-45 seconds and swirl; return to the bath for more softening and remove after an additional 30-45 seconds for more swirling; repeat the heating-swirling process until all the tarry residue has been liquified and mixed with the propylene glycol (2 to 3 minutes of total heating time).

c. Measure out 17.5 ml of saline vehicle in a sterile 25 ml measuring vessel; re-cover the beaker and measuring vessel with foil and set the measured volume of saline next to the mixer in the hood.

d. Place the mixing vessel under the probe so that the probe reaches as far into the vessel as possible; mix the warm extract-propylene glycol at SPEED 5 for approximately 30 seconds before starting to pour in the saline.

e. Pour the saline slowly into the extract-propylene glycol while the mixer is running; once sufficient saline has been added to raise the emulsion volume beyond the bottom of the last slot of the probe, begin the side-to-side and up-and-down motion of the mixing vessel (to insure complete mixing of components) while still continuing to pour the saline in (i.e., one hand holds the mixing vessel while the other hand pours the saline from the measuring vessel).

Note: The spinning motion of the probe components creates a sucking action that pulls the mixing vessel up tightly against the probe; the mixing vessel should not be allowed to remain sucked up against the probe for more than a few seconds at a time.

f. Once all the saline has been added, increase the mixing speed to 6 and continue mixing for 1 to 2 minutes with constant motion of the vessel; mixing is complete when the emulsion has achieved its lightest color.

PREPARATION OF DIESEL EXTRACT AND Fe_2O_3 EMULSIONS (continued)

   g. Remove the mixing vessel from the probe and wick-off the excess emulsion from the probe with the sides of the mixing vessel.

   h. Add the weighed iron oxide and mix at SPEED 6 for 1 to 2 minutes; leave the probe fully immersed in the emulsion when the mixer is shut off.

   i. Remove the mixing vessel from the probe and wick-off the extra emulsion.

   j. Immediately pour the emulsion into a labeled glass collection vessel; replace the foil cover on the collection vessel.

   k. Proceed with the next concentration--steps 4a through 4k--until all concentrations of the diesel extract have been mixed.

5. Tear off the foil wrapping from the collection vessel lids, one at a time.

   a. Unwrap the plastic cap for the control and set the opening side down on top of the foil until the foil has been quickly lifted off the plastic bottle mouth; set the cap on the bottle mouth and quickly screw down.

   b. Unwrap the glass stopper by first unwrapping the "handle" end of the stopper so it may be held in one hand while the other hand quickly tears off the foil from the stopper end and then lifts the foil off the mouth of the glass collection vessel; quickly place the stopper in the collection vessel.

6. Rinse the probe with solvent (acetone) from a wash bottle and capture the rinse in a used mixing vessel.

   a. Pour the rinse into the toxic waste container in the hood.

   b. Repeat the probe rinse-capture operations until the solvent dripping from the probe is clear.

c. Rinse the probe with clean distilled water by mixing a fresh portion of distilled water for 2 to 3 minutes in a clean 100 or 250 ml mixing vessel at SPEED 6.

7. Rinse the other mixing vessels used for emulsion preparation with solvent and pour the rinse into the waste container in the hood.

8. Place the dirty glassware in the sink for washing.

9. Remove the probe from the mixer and clean it immediately.

10. Make and affix paper labels to each container with the sequential preparation number assigned from the project logbook, prep. type, component concentrations, prep. person, and prep. date.

11. Deliver the emulsions and control to the materials users.

PREPARATION OF CIGARETTE SMOKE CONDENSATE AND Fe_2O_3 EMULSIONS

STARTING MATERIALS (see RAW MATERIALS list, p. 11 & 12)

CSC: appropriate phase "stock" material
"working" solution is "stock" solution which is ∿216 mg/ml in acetone and is stored in 3F1-1,2 refrigerator freezer

Vehicle: saline with:
0.5% wt/vol gelatin
0.25% wt/vol gum arabic
propylene glycol (added at 10% vol/vol) with 0.5% wt/vol gum arabic in suspension

Iron Oxide: synthetic hematite

EMULSION CONCENTRATIONS

CSC and Fe_2O_3, each present in 5, 2.5 and 1.25 mg per 0.2 ml emulsions, prepared individually at volumes of 20 ml each

Control - 20 ml of 5 mg Fe_2O_3 per 0.2 ml vehicle

Note: Controls for CSC and Coke Oven are combined and mixed as one, then split in half for delivery.

PREPARATION SCHEDULE

Prepared fresh every week not less than 2 hours nor more than 18 hours before needed--i.e., prepared late Tuesday

TOTAL CONDENSATE MASS AND TOTAL CONDENSATE "WORKING" SOLUTION WEEKLY REQUIREMENTS

875 mg condensate = 4.2 ml of "working" solution

GLASSWARE, PLASTICWARE REQUIREMENTS (see glassware prep. schedule, p. 14)

25 ml mixing vessel for CSC emulsions - 1 for each concentration

100 ml mixing vessel - for mixing combined CSC and coke oven Fe_2O_3 control

5 ml measuring vessel - 1

25 ml measuring vessel - 2

PREPARATION OF CIGARETTE SMOKE CONDENSATE AND Fe_2O_3 EMULSIONS (continued)

50 ml glass collection vessels - 1 per concentration

30 ml plastic collection vessels - 2 for combined control that is split in half

extra 100 ml, 250 ml mixing vessels for probe cleaning

HARDWARE REQUIREMENTS

Same as for the diesel extract emulsions

NO PREPARATION OF "WORKING" SOLUTION IS REQUIRED

PREPARATION OF GLASSWARE, VEHICLE AND CONDENSATE FOR THE EMULSIFICATION

1. Check the schedule for the required glassware, vehicle volume and weighed iron oxide portions required. Prepare and autoclave glassware and vehicle according to instructions in "Glassware and Vehicle Preparation for Autoclaving" and "Autoclaving Glassware and Vehicle".

   Note: The preparation schedule is arranged so that sufficient glassware and vehicle are prepared for this emulsion as well as the coke oven extract emulsion.

2. Fully dry the mixing vessels.
   - a. Rinse with ethanol
   - b. Dry in the laboratory oven (80°C)
   - c. Cool to room temperature in a desiccator
   - d. Equilibrate to ambient humidity conditions (30 minutes outside of the desiccator, once cooled)

3. Remove the "working" solution from the refrigerator freezer (CRB 3F1-1,2) and allow it to come to room temperature.

   Note: Acetone expands considerably in volume in going from freezer temperature to room temperature.

4. Label and weigh the mixing vessels on the METTLER analytical balance to the nearest 0.1 mg (see the SOP for this balance); record these weights in the laboratory logbook.

5. Measure out the required volumes of the "working" solution into the mixing vessels with the 5 ml graduate cylinder designated for for the CSC.

   a. 0.6 ml - for the 1.25 mg per 0.2 ml emulsion

   b. 1.2 ml - for the 2.5 mg per 0.2 ml emulsion

   c. 2.4 ml - for the 5.0 mg per 0.2 ml emulsion

6. Turn the hot plate on to the MEDIUM setting and place a (large crystallizing) dish of water--two-thirds full--on the hot plate.

7. Blow the solvent off the "working" solution of CSC that has been measured into the mixing vessels.

   a. Place each mixing vessel below the nitrogen delivery tubes in the hood (no. 98, CRB 3F1-1,2)

   b. Insert a clean pasteur pipette in the end of each nitrogen delivery tube that is to be used.

   c. Insert the pasteur pipettes into each mixing vessel and adjust the tubing length (by sliding the tubing up or down in the 3-prong holding clamp) so that the pipette is approximately one-quarter inch above the solution surface.

   d. Check the nitrogen cylinder and regulator setting to see if:

      d_1 the tank valve is open

      d_2 there is sufficient nitrogen in the tank (change the tank if empty according to the posted SOP above the cylinder rack)

      d_3 the regulator valve is set to 15-20 psi

e. Open the delivery stream valve to start the flow of nitrogen.

Note: Opening this valve will drop the regulator pressure to 10-15 psi, which is satisfactory.

f. Check the delivery of the nitrogen to the mixing vessels.

f_1 Insure that the flow rate is not too fast to cause splashing and loss of some of the CSC solution--raise the pipette if this is the case.

f_2 The pipette must be checked during the entire course of the blow-down (30 to 45 minutes) so that it can be lowered as the solution level drops.

Note: A thick layer of CSC may develop and prevent the nitrogen stream from removing all the solvent; break this layer by manually moving the nitrogen stream over the surface of the extract, concentrating it near the center, then the sides.

g. The solvent removal is complete when the mixing vessel returns to room temperature (evaporation of the solvent makes the mixing vessel cold).

h. Turn off the nitrogen delivery stream valve and remove the pipettes from the vessels.

8. Return to the METTLER analytical balance and reweigh the mixing vessels which now contain the CSC with solvent.

   a. Follow the SOP for using the balance.

   b. Record the vessel + CSC weight above the empty vessel weight previously recorded (step 4).

c. Subtract the empty vessel weight from the vessel + CSC weight to yield the weight of the CSC.

Note: The extract weight should be ±10% of the desired weight; if the extract weight is outside of this 10% range, add more extract (remembering to blow-off the new solvent now added) or calculate how much larger the total emulsion volume must be to yield the desired mg per 0.2 ml dose (remembering to also increase the volume of propylene glycol and the weight of the iron oxide that must be added to the emulsion).

9. Pour the measured 250 mg of gum arabic into the sterilized 50 ml of propylene glycol and swirl to form a suspension.

10A. Measure 2 ml of propylene glycol-gum arabic (with the 5 ml measuring vessel) into each mixing vessel containing CSC.

Note: 2.5 ml must be measured and poured out until the fluid stream stops in order to deliver 2 ml.

10B. Measure 4 ml of propylene glycol-gum arabic (with the 5 ml measuring vessel) into 100 ml mixing vessel to be used for preparing combined CSC-coke oven Fe_2O_3 control.

Note: 5 ml must be measured and poured out until the fluid stream stops in order to deliver 4 ml.

11. Pour saline vehicle into the 100 ml control suspension mixing vessel up to the 40 ml line, and re-cover the saline and the mixing vessel with foil.

PREPARATION OF CIGARETTE SMOKE CONDENSATE AND Fe_2O_3 EMULSIONS (continued)

12. Match-up the mixing vessels, labeled collection vessels, and pans of Fe_2O_3 (remove covers and inspect to insure that labels of amounts were accurate) in a line on the lab bench closest to hood no. 97 where the mixing is to occur.

MIXING THE CSC EMULSIONS AND CONTROL WITH THE POLYTRON®

1. Attach the clean PT-10ST probe generator to the mixing unit (see instrument instruction manual).
   a. Rinse with 10-20 ml 100% ethanol from a wash bottle and discard this rinse.
   b. Fill a sterile spare mixing vessel (100 or 250 ml) two-thirds full with sterile distilled water.
   c. Mix at SPEED 6 for 2-3 minutes.
   d. Wick-off the water with the sides of the mixing vessel.
   e. Re-cover the mixing vessel of sterile water with foil.

2. Mix the control suspension (vehicle only) for 1-2 minutes at SPEED 6.
   a. Add the weighed iron oxide.
   b. Mix 1-2 minutes at SPEED 6.
   c. Wick-off the excess suspension with the sides of the mixing vessel.
   d. Immediately pour the control suspension into plastic collection vessels and re-cover the collection vessels with foil.

3. Rinse the probe in a fresh portion of sterile water by mixing at SPEED 6 for 1-2 minutes; wick-off the excess water with the sides of the mixing vessel.

PREPARATION OF CIGARETTE SMOKE CONDENSATE AND Fe_2O_3 EMULSIONS (continued)

4. Mix the condensates, beginning with the 1.25 mg/0.2 ml concentration.

   a. First swirl the mixing vessel to mix the propylene glycol with the semi-solid CSC.

   b. Set the mixing vessel in the hot (80°C) water bath to soften the semi-solid phase of the CSC; remove from the bath every 30-45 seconds and swirl; return to the bath for more softening and remove after an additional 30-45 seconds for more swirling; repeat the heating-swirling process until all the semi-solid CSC has been liquified and mixed with the propylene glycol (2 to 3 minutes of total heating time).

   c. Measure out 17.5 ml saline vehicle in a sterile 25 ml measuring vessel; re-cover the beaker and measuring vessel with foil and set the measured volume of saline next to the mixer in the hood.

   d. Place the mixing vessel under the probe so that the probe reaches as far into the vessel as possible; mix the warm condensate-propylene glycol at SPEED 5 for approximately 30 seconds before starting to pour in the saline.

   e. Pour the saline slowly into the condensate-propylene glycol while the mixer is running; once sufficient saline has been added to raise the emulsion volume beyond the bottom of the last slot of the probe, begin the side-to-side and up-and-down motion of the mixing vessel (to insure complete mixing of components) while still continuing to pour the saline in (i.e., one hand holds the mixing vessel while the other hand pours the saline from the measuring vessel).

      Note: The spinning motion of the probe components creates a sucking action that pulls the mixing vessel up tightly against the probe; the mixing vessel should not be allowed to remain sucked up against the probe for more than a few seconds at a time.

f. Once all the saline has been added, increase the mixing speed to 8 and continue mixing for 1 to 2 minutes with constant motion of the vessel; mixing is complete when the emulsion has achieved its lightest color.

g. Remove the mixing vessel from the probe and wick-off the excess emulsion from the probe with the sides of the mixing vessel.

h. Add the weighed iron oxide and mix at SPEED 6 for 1 to 2 minutes; leave the probe fully immersed in the emulsion when the mixer is shut off.

i. Remove the mixing vessel from the probe and wick-off the extra emulsion.

j. Immediately pour the emulsion into a labeled glass collection vessel; replace the foil cover on the collection vessel.

k. Proceed with the next concentration--steps 4a through 4k--until all concentrations of the CSC-Fe_2O_3 have been mixed.

5. Tear off foil wrapping from the collection vessel lids, one at a time.

   a. Unwrap the plastic cap for the control and set the opening side down on top of the foil until the foil has been quickly lifted off the plastic bottle mouth; set the cap on the bottle mouth and quickly screw down.

   b. Unwrap the glass stopper by first unwrapping the "handle" end of the stopper so it may be held in one hand while the other hand quickly tears off the foil from the stopper end and then lifts the foil off the mouth of the glass collection vessel; quickly place the stopper in the collection vessel.

6. Rinse the probe with solvent (acetone) from a wash bottle and capture the rinse in a used mixing vessel.
   a. Pour the rinse into the toxic waste container in the hood.
   b. Repeat the probe rinse-capture operations until the solvent dripping from the probe is clear.
   c. Rinse the probe with clean distilled water by mixing a fresh portion of distilled water for 2 to 3 minutes in a clean 100 or 250 ml mixing vessel at SPEED 6.

7. Rinse the other mixing vessels used for emulsion preparation with solvent and pour the rinse into the waste container in the hood.

8. Place all the dirty glassware in the sink for washing.

9. Remove the probe from the mixer and clean it immediately.

10. Make and affix paper labels to each container with the sequential preparation number assigned from the project logbook, prep. type, component concentrations, prep. person, and prep. date.

    Note: Labels for the two bottles from the combined batch of the Fe_2O_3 control should be given the same prep. number but marked -1 and -2 to indicate that the two bottles of control are halves of one preparation.

11. Continue with preparation of the coke oven extract emulsions before delivering the emulsions to the materials users.

PREPARATION OF COKE OVEN EXTRACT AND Fe_2O_3 EMULSIONS

STARTING MATERIALS (see RAW MATERIALS list, p. 11 & 12)

CO:	appropriate phase "stock" solution "working" solution of 125 mg/ml for each phase and is stored in 3F1-1,2 refrigerator freezer
Vehicle:	saline with: 0.5% wt/vol gelatin 0.25% wt/vol gum arabic propylene glycol (added at 10% vol/vol) with 0.5% wt/vol gum arabic in suspension
Iron Oxide:	synthetic hematite

EMULSION CONCENTRATIONS

CO and Fe_2O_3, each present in 5, 2.5 and 1.25 mg per 0.2 ml emulsions, prepared individually at volumes of 20 ml each

Control - 20 ml of 5 mg Fe_2O_3 per 0.2 ml vehicle

Note: CO control suspension is prepared with CSC control but is bottled separately from CSC control for delivery.

PREPARATION SCHEDULE

Prepared fresh each week not less than 4 hours nor more than 18 hours before needed--i.e., prepared late Tuesday.

TOTAL CO EXTRACT MASS AND TOTAL CO "WORKING" SOLUTION REQUIRED WEEKLY

875 mg CO extract = 7 ml of "working" solution

GLASSWARE, PLASTICWARE REQUIREMENTS (see glassware prep. schedule, p. 14)

25 ml mixing vessel for CO emulsions - 1 for each concentration
5 ml measuring vessel - 1
25 ml measuring vessel - 2
50 ml glass collection vessel - 1 per concentration
extra 100 ml, 250 ml mixing vessels for probe cleaning

PREPARATION OF COKE OVEN EXTRACT AND Fe_2O_3 EMULSIONS (continued)

HARDWARE REQUIREMENTS

Same as for the diesel extract emulsions.

PREPARATION OF THE "WORKING" SOLUTION FROM THE "STOCK" SOLUTION

(125 mg/ml solution from known and unknown concentration "stock" solutions)

1. Phase I - "stock" solution has been determined to be 161.4 mg/ml.
    a. Remove Phase I "stock" solution from low temperature freezer and allow it to come to room temperature.
    b. Pipette 77.4 ml of "stock" solution into 100 ml volumetric flask.

        1 x 50 ml

        1 x 25 ml

        1 x 2.4 ml transfer pipette

    c. Dilute to 100 ml with methylene chloride and shake vigorously, carefully venting built-up vapors occasionally.

        Note: A second "working" solution will have to be prepared 2-3 weeks before the end of the phase.

    d. Return the "stock" solution to the low temperature freezer.
    e. Place the prepared CO "working" solution for Phase I in the refrigerator freezer in 3F1-1,2 until needed.

2. Phase II - "stock" solution concentration is unknown.
    a. Remove Phase II "stock" solution from the low temperature freezer and allow it to come to room temperature.
    b. Weigh a clean, empty foil weighing pan on the METTLER analytical balance = pan tare weight.
    c. Pipette 1.0 ml of Phase II "stock" solution into the empty pan.

PREPARATION OF COKE OVEN EXTRACT AND Fe_2O_3 EMULSIONS (continued)

d. Blow-off the methylene chloride solvent with nitrogen.

e. Reweigh the pan containing the solvent-free CO extract.

f. Subtract the pan tare weight from the pan + CO extract weight; the difference is the mass of the CO extract per ml of solvent.

g. Determine the number of mls of Phase II "stock" solution required to yield 12,500 mg of extract from the "stock" solution concentration determined in a through f above; 12,500 mg ÷ determined mg/ml = number of mls of Phase II "stock" solution that should be pipetted into a 100 ml volumetric flask; pipette this volume out.

h. Fill the 100 ml volumetric flask containing the pipetted volume of Phase II "stock" solution to the 100 ml mark with methylene chloride; shake to complete the preparation of the "working" solution.

   Note: A second "working" solution will have to be prepared 2-3 weeks before the end of the phase.

i. Return the "stock" solution for Phase II to the low temperature freezer.

j. Place the prepared CO "working" solution for Phase II in the refrigerator freezer in 3F1-1,2 until needed.

PREPARATION OF GLASSWARE, VEHICLE AND EXTRACT FOR THE EMULSIFICATION

1. The glassware and vehicle for the CO emulsions should have been prepared with the cigarette smoke condensate glassware.

2. Fully dry the mixing vessels.
   a. Rinse with ethanol
   b. Dry in the laboratory oven (80°C)

PREPARATION OF COKE OVEN EXTRACT AND Fe_2O_3 EMULSIONS (continued)

   c. Cool to room temperature in a desiccator

   d. Equilibrate to ambient humidity conditions (30 minutes outside of the desiccator, once cooled)

3. Remove the "working" solution from the refrigerator freezer (CRB 3F1-1,2) and allow it to come to room temperature.

   Note: Methylene chloride expands considerably in volume in going from freezer temperature to room temperature.

4. Label and weigh the mixing vessels on the METTLER analytical balance to the nearest 0.1 mg (see the SOP for this balance); record these weights in the laboratory logbook.

5. Measure out the required volumes of the "working" solution into the mixing vessels with the labeled pipettes kept in hood no. 97.

   a. 1 ml - for the 1.25 mg/0.2 ml emulsion

   b. 2 ml - for the 2.5 mg/0.2 ml emulsion

   c. 4 ml - for the 5 mg/0.2 ml emulsion

6. Turn the hot plate on to the MEDIUM setting and place a (large crystallizing) dish of water--two-thirds full--on the hot plate.

7. Blow the solvent off the "working" solution of extract that has been measured into the mixing vessels.

   a. Place each mixing vessel below the nitrogen delivery tubes in the hood (no. 98, CRB 3F1-1,2).

   b. Insert a clean pasteur pipette in the end of each nitrogen delivery tube that is to be used.

c. Insert the pasteur pipettes into each mixing vessel and adjust the tubing length (by sliding the tubing up or down in the 3-prong holding clamp) so that the pipette is approximately one-quarter inch above the solution surface.

d. Check the nitrogen cylinder and regulator setting to see if:

   d_1 the tank valve is open

   d_2 there is sufficient nitrogen in the tank (change the tank if empty according to the posted SOP above the cylinder rack)

   d_3 the regulator valve is set to 15-20 psi

e. Open the delivery stream valve to start the flow of nitrogen.

   Note: Opening this valve will drop the regulator pressure to 10-15 psi, which is satisfactory.

f. Check the delivery of the nitrogen to the mixing vessels.

   f_1 Insure that the flow rate is not too fast to cause splashing and loss of some of the extract solution--raise the pipette if this is the case.

   f_2 The pipette must be checked during the entire course of the blow-down (30 to 45 minutes) so that it can be lowered as the solution level drops.

   Note: A thick layer of extract may develop and prevent the nitrogen stream from removing all the solvent; break this layer by manually moving the nitrogen stream over the surface of the extract, concentrating it near the center, then the sides.

g. The solvent removal is complete when the mixing vessel returns to room temperature (evaporation of the solvent makes the mixing vessel cold).

h. Turn off the nitrogen delivery stream valve and remove the pipettes from the vessels.

8. Return to the METTLER analytical balance and reweigh the mixing vessels which now contain the extract without solvent.

   a. Follow the SOP for using the balance.

   b. Record the vessel + extract weight above the empty vessel weight previously recorded (step 4).

   c. Subtract the empty vessel weight from the vessel + extract weight to yield the weight of the extract.

   Note: The extract weight should be ±10% of the desired weight; if the extract weight is outside of this 10% range, add more extract (remembering to blow-off the new solvent now added) or calculate how much larger the total emulsion volume must be to yield the desired mg per 0.2 ml dose (remembering to also increase the volume of propylene glycol and the weight of the iron oxide that must be added to the emulsion).

9. Pour the measured 250 mg of gum arabic into the sterilized 50 ml of propylene glycol and swirl to form a suspension.

10. Measure 2 ml of propylene glycol-gum arabic (with 5 ml measuring vessel) into each mixing vessel containing extract.

    Note: Propylene glycol is viscous and will adhere to the walls of the measuring vessel; therefore, measure out 2.5 ml and pour the propylene glycol out until the fluid stream stops; do not allow the propylene to continue to drip out; upon returning the measuring vessel to the upright position, it will be observed that 0.5 ml of propylene glycol remains and therefore 2.0 ml was delivered to the mixing vessel.

PREPARATION OF COKE OVEN EXTRACT AND Fe_2O_3 EMULSIONS (continued)

11. Match-up the mixing vessels, labeled collection vessels, and pans of iron oxide in a line on the lab bench closest to the hood in which the mixer is located.

    Note: Remove the foil covers from the labeled pans of iron oxide and inspect the contents to insure they contain the quantities indicated on the label--i.e., the 2.5 mg pan contains twice as much as the 1.25 mg pan but only half as much as the 5 mg pan.

MIXING THE CO EMULSIONS WITH THE POLYTRON®

1. Heat the saline in the hot water bath to 80°C.
    a. Measure two 17.5 ml portions of saline into each of the two remaining 25 ml measuring vessels; re-cover vessels and beaker (with remaining saline solution) with foil.
    b. Place measuring vessels and beaker with saline solution in the hot water bath 30 minutes before use.

2. Attach the clean PT-10ST probe generator to the mixing unit (see instrument instruction manual).
    a. Rinse with 10-20 ml of 100% ethanol from a wash bottle and discard this rinse.
    b. Fill a sterile spare mixing vessel (100 or 250 ml) two-thirds full with sterile distilled water.
    c. Mix at SPEED 6 for 2-3 minutes.
    d. Wick-off the water with the sides of the mixing vessel.
    e. Re-cover the mixing vessel of sterile water with foil.

3. Mix the extracts, beginning with the 1.25 mg/0.2 ml emulsion.

   a. Place the mixing vessel in the hot water bath until the tarry material adhering to the walls of the mixing vessel are visually observed to melt and flow to the bottom of the vessel; swirl every 45 to 60 seconds to increase the rate of softening of the tar.

      Note: The hot water in the bath must be at least 0.5 inches above the tar line in the CO mixing vessel.

   b. Immediately after the melt has occurred, add one-half the volume of the heated saline vehicle from one of the measuring vessels to the mixing vessel; re-cover the measuring vessel with foil and return it to the hot water bath.

      Note: The liquid (propylene glycol) above the melted tar will turn a light yellow color as the hot saline is added.

   c. Place the mixing vessel under the probe so that the probe reaches as far as possible into the vessel; mix the hot material at SPEED 7 for 1-2 minutes with much side-to-side and up-and-down motion of the mixing vessel.

   d. With the mixer still running, add the remaining portion of the hot saline vehicle.

   e. Turn up the mixer speed to 8 and mix an additional 2-3 minutes with constant motion of the mixing vessel.

      Note: This material foams vigorously and mixing should be halted before the emulsion spills over the top of the vessel; beware that the mixing vessel is hot to begin with and will get hotter during the course of the mixing.

   f. Shut off the mixer with the probe still fully immersed in the emulsion; wick-off excess emulsion from the probe with the sides of the mixing vessel.

PREPARATION OF COKE OVEN EXTRACT AND Fe_2O_3 EMULSIONS (continued)

   g. Add the iron oxide and mix at SPEED 8 for 1-2 minutes; leave the probe fully immersed in the emulsion when the mixer is shut off.

   h. Remove the mixing vessel from the probe and wick-off the extra emulsion.

   i. Immediately pour the emulsion into a labeled glass collection vessel; replace the foil cover on the collection vessel.

   j. Proceed with the next concentration--steps 3a through 3i--until all concentrations of the CO-Fe_2O_3 have been mixed.

4. Tear off the foil wrapping from the collection vessel glass stoppers, one at a time; unwrap the glass stoppers by first unwrapping the "handle" end of the stopper so it may be held in one hand while the other hand quickly tears off the foil from the stopper end and then lifts the foil off the foil off the mouth of the glass collection vessel; quickly place the stopper in the collection vessel.

5. Rinse the probe with solvent (acetone) from a wash bottle and capture the rinse in a used mixing vessel.

   a. Pour the rinse into the toxic waste container in the hood.

   b. Repeat the probe rinse-capture operations until the solvent dripping from the probe is clear.

   c. Rinse the probe with clean distilled water by mixing a fresh portion of distilled water for 2 to 3 minutes in a clean 100 or 250 ml mixing vessel at SPEED 6.

6. Rinse the other mixing vessels used for emulsion preparation with solvent and pour the rinse into the waste container in the hood.

PREPARATION OF COKE OVEN EXTRACT AND Fe_2O_3 EMULSIONS (continued)

7. Place the dirty glassware in the sink for washing.

8. Remove the probe from the mixer and clean it immediately.

9. Make and affix paper labels to each container with the sequential preparation number assigned from the project logbook, prep. type, component concentrations, prep. person, and prep. date.

10. Deliver the cigarette smoke condensate and coke oven extract emulsions, and the controls to the materials users.

PREPARATION OF ROOFING TAR (ASPHALT) EXTRACT AND Fe_2O_3 EMULSIONS

STARTING MATERIALS (see RAW MATERIALS list, p. 11 & 12)

RT:	appropriate phase "stock" solution from which "working" solution of 125 mg/ml has been prepared
Vehicle:	saline with: 0.5% wt/vol gelatin 0.25% wt/vol gum arabic propylene glycol (added at 10% vol/vol) with 0.5% wt/vol gum arabic in suspension
Iron Oxide:	synthetic hematite

EMULSION CONCENTRATIONS

RT and Fe_2O_3, each present in 5, 2.5 and 1.25 mg per 0.2 ml emulsions, prepared individually at volumes of 20 ml each

Control - 20 ml of 5 mg Fe_2O_3 per 0.2 ml vehicle

PREPARATION SCHEDULE

Prepared fresh each week not less than 2 hours nor more than 18 hours before needed--i.e., prepared late Wednesday.

QUANTITIES OF RT NEEDED WEEKLY

875 mg RT extract = 7 ml of "working" solution

GLASSWARE, PLASTICWARE REQUIREMENTS (see glassware prep. schedule, p. 14)

25 ml mixing vessel - 3 for RT emulsions; 1 for control
5 ml measuring vessel - 1
25 ml measuring vessel - 2
50 ml glass collection vessel - 3 for RT emulsions
30 ml plastic collection vessel - 1 for control
extras of above, plus 100 ml and 250 ml mixing vessels for probe cleaning

PREPARATION OF ROOFING TAR (ASPHALT) EXTRACT AND Fe_2O_3 EMULSIONS (cont.)

HARDWARE REQUIREMENTS

Same as for the diesel extract emulsions

PREPARATION OF THE "WORKING" SOLUTION FROM THE "STOCK" SOLUTION

1. Remove one bottle of the appropriate phase "stock" solution (200 mg/ml) from the low temperature freezer and allow the solution to come to room temperature.

2. Pipette 62.5 ml of the "stock" solution into a 100 ml volumetric flask.

   a. 1 x 50 ml pipette

   b. 1 x 10 ml pipette

   c. a 5.0 ml transfer pipette filled and then drained to 2.5 ml (discard the remainder of the solution in the pipette by draining it into the toxic waste vessel in the hood)

3. Fill the 100 ml volumetric flask with methylene chloride to the indicating line to produce a 125 mg/ml "working" solution.

   Note: A second "working" solution will have to be prepared 2 to 3 weeks before the end of the phase.

4. Stopper the flask and gently shake to complete the preparation of the "working" solution.

   Note: Carefully loosen then remove the stopper to vent the vapors that have built up from the shaking action.

5. Return the "stock" solution to the low temperature freezer.

6. Label the "working" solution and place it in the refrigerator freezer in CRB 3F1-1,2 until it is needed.

PREPARATION OF ROOFING TAR (ASPHALT) EXTRACT AND Fe_2O_3 EMULSIONS (cont.)

PREPARATION OF GLASSWARE, VEHICLE AND EXTRACT FOR THE EMULSIFICATION

1. Check the schedule for the required glassware, vehicle volume, and weighed iron oxide portions required. Prepare and autoclave glassware and vehicle according to instructions in "Glassware and Vehicle Preparation for Autoclaving" and "Autoclaving Glassware and Vehicle".

2. Fully dry the mixing vessels.
    a. Rinse with ethanol
    b. Dry in the laboratory oven (80°C)
    c. Cool to room temperature in a desiccator
    d. Equilibrate to ambient humidity conditions (30 minutes outside of the desiccator, once cooled)

3. Remove the "working" solution from the refrigerator freezer (CRB 3F1-1,2) and allow it to come to room temperature.

    Note: Methylene chloride expands considerably in volume in going from freezer temperature to room temperature.

4. Label and weigh the mixing vessels on the METTLER analytical balance to the nearest 0.1 mg (see the SOP for this balance); record these weights in the laboratory logbook.

5. Measure out the required volumes of the "working" solution into the mixing vessels with the labeled pipettes kept in hood no. 97.
    a. 1 ml - for the 1.25 mg per 0.2 ml emulsion
    b. 2 ml - for the 2.5 mg per 0.2 ml emulsion
    c. 4 ml - for the 5.0 mg per 0.2 ml emulsion

6. Turn the hot plate on to the MEDIUM setting and place a (large crystallizing) dish of water--two-thirds full-- on the hot plate.

PREPARATION OF ROOFING TAR (ASPHALT) EXTRACT AND Fe_2O_3 EMULSIONS (cont.)

7. Blow the solvent off the "working" solution of extract that has been measured into the mixing vessels.

   a. Place each mixing vessel below the nitrogen delivery tubes in the hood (no. 98, CRB 3F1-1,2).

   b. Insert a clean pasteur pipette in the end of each nitrogen delivery tube that is to be used.

   c. Insert the pasteur pipettes into each mixing vessel and adjust the tubing length (by sliding the tubing up or down in the 3-prong holding clamp) so that the pipette is approximately one-quarter inch above the solution surface.

   d. Check the nitrogen cylinder and regulator settings to see if:

      d_1 the tank valve is open

      d_2 there is sufficient nitrogen in the tank (change the tank if empty according to the posted SOP above the cylinder rack)

      d_3 the regulator valve is set to 15-20 psi

   e. Open the delivery stream valve to start the flow of nitrogen.

      Note: Opening this valve will drop the regulator pressure to 10-15 psi, which is satisfactory.

   f. Check the delivery of the nitrogen to the mixing vessels.

      f_1 Insure that the flow rate is not too fast to cause splashing and loss of some of the extract solution--raise the pipette if this is the case.

      f_2 The pipette must be checked during the entire course of the blow-down (30 to 45 minutes) so that it can be lowered as the solution level drops.

      Note: A thick layer of extract may develop and prevent the nitrogen stream from removing all the solvent;

break this layer by manually moving the nitrogen stream over the surface of the extract, concentrating it near the center, then the sides.

g. The solvent removal is complete when the mixing vessel returns to room temperature (evaporation of the solvent makes the mixing vessel cold).

h. Turn off the nitrogen delivery stream valve and remove the pipettes from the vessels.

8. Return to the METTLER analytical balance and reweigh the mixing vessels which now contain the extract without solvent.

   a. Follow the SOP for using the balance.

   b. Record the vessel + extract weight above the empty vessel weight previously recorded (step 4).

   c. Subtract the empty vessel weight from the vessel + extract weight to yield the weight of the extract.

   Note: The extract weight should be ±10% of the desired weight; if the extract weight is outside of this 10% range, add more extract (remembering to blow-off the new solvent now added) or calculate how much larger the total emulsion volume must be to yield the desired mg per 0.2 ml dose (remembering to also increase the volume of propylene glycol and the weight of the iron oxide that must be added to the emulsion).

9. Pour the measured 250 mg of gum arabic into the sterilized 50 ml of propylene glycol and swirl to form a suspension.

PREPARATION OF ROOFING TAR (ASPHALT) EXTRACT AND Fe_2O_3 EMULSIONS (cont.)

10. Measure 2 ml of propylene glycol-gum arabic (with the 5 ml measuring vessel) into each mixing vessel containing extract and into an empty, sterile 25 ml mixing vessel (for preparation of the control).

    Note: Propylene glycol is viscous and will adhere to the walls of the measuring vessel; therefore, measure out 2.5 ml and pour the propylene glycol out until the fluid stream stops; do not allow the propylene glycol to continue to drip out; upon returning the measuring vessel to the upright position, it will be observed that 0.5 ml of propylene glycol remains and therefore 2.0 ml was delivered to the mixing vessel.

11. Measure 18 ml of saline vehicle with a 25 ml measuring vessel and pour it into the control suspension mixing vessel.

12. Match-up the mixing vessels, labeled collection vessels, and pans of iron oxide in a line on the lab bench closest to the hood in which the mixer is located (hood no. 97).

    Note: Remove the foil covers from the labeled pans of iron oxide and inspect the contents to insure they contain the quantities indicated on the label--i.e., the 2.5 mg pan contains twice as much as the 1.25 mg pan but only half as much as the 5 mg pan.

MIXING THE ROOFING TAR EXTRACT EMULSIONS AND CONTROL WITH THE POLYTRON®

1. Attach the clean PT-10ST probe generator to the mixing unit (see instrument instruction manual) and sterilize.

    a. Rinse with 10-20 ml of 100% ethanol from a wash bottle and discard this rinse.

    b. Fill a sterile spare mixing vessel (100 or 250 ml) two-thirds full with sterile distilled water.

    c. Mix at SPEED 6 for 2-3 minutes.

   d. Wick-off the water with the sides of the mixing vessel.
   e. Re-cover the mixing vessel of sterile water with foil.

2. Mix the control suspension (vehicle only) for 1-2 minutes at SPEED 6.
   a. Add the weighed iron oxide.
   b. Mix 1-2 minutes at SPEED 6.
   c. Wick-off the excess suspension with the sides of the mixing vessel.
   d. Immediately pour the control suspension into a plastic collection vessel and re-cover the collection vessel with foil.

3. Rinse the probe in a fresh portion of sterile water by mixing at SPEED 6 for 1-2 minutes; wick-off the excess water with the sides of the mixing vessel.

4. Dry the probe by rinsing with 100% ethanol and then wiping with a clean paper towel.

5. Mix the extracts, beginning with the 1.25 mg/0.2 ml concentration.
   a. First swirl the mixing vessel to wet the RT extract with the propylene glycol.

      Note: The RT adheres to the walls of the mixing vessel as far up as the original "working" solution was present.

   b. Set the mixing vessel in the hot (80°C) water bath to soften the semi-solid RT extract; remove from the bath every 30 to 45 seconds and swirl; return to the bath for more softening and remove after an additional 30-45 seconds for more swirling; repeat the heating-swirling process until all the waxy residue has been liquified and mixed as well as possible with the propylene glycol (2 to 3 minutes of total heating time).

Note: Very little of the RT is miscible with the propylene glycol.

c. Measure out 17.5 ml of saline vehicle in a sterile 25 ml measuring vessel; re-cover the beaker and measuring vessel with foil and set the measured volume of saline in the hot water bath.

d. Place the mixing vessel under the probe so that the probe reaches as far into the vessel as possible; mix the warm extract-propylene glycol at SPEED 8 for approximately 60 seconds.

e. Remove the vessel from the probe and wick-off the excess emulsion from the probe with the sides of the mixing vessel.

f. Add the iron oxide and mix at SPEED 8 for approximately 30 seconds.

g. Pour the saline slowly into the extract-propylene glycol while the mixer is running; once sufficient saline has been added to raise the emulsion volume beyond the bottom of the last slot of the probe, begin the side-to-side and up-and-down motion of the mixing vessel (to insure complete mixing of components) while still continuing to pour the saline in (i.e., one hand holds the mixing vessel while the other hand pours the saline from the measuring vessel).

Note: The spinning motion of the probe components creates a sucking action that pulls the mixing vessel up tightly against the probe; the mixing vessel should not be allowed to remain sucked up against the probe for more than a few seconds at a time.

h. Once all the saline has been added, increase the mixing speed to the maximum and continue mixing for 3 to 4 minutes with constant motion of the vessel.

PREPARATION OF ROOFING TAR (ASPHALT) EXTRACT AND Fe_2O_3 EMULSIONS (cont.)

- i. Remove the mixing vessel from the probe and wick-off the excess emulsion from the probe with the sides of the mixing vessel.
- j. Immediately pour the emulsion into a labeled glass collection vessel; replace the foil cover on the collection vessel.
- k. Rinse the probe with 100% ethanol and wipe the probe with a paper towel to dry it before proceeding with the next concentration.
- l. Proceed with the next concentration--steps 5a through 5k--until all concentrations of the RT emulsions have been mixed.

6. Tear off the foil wrapping from the collection vessel lids, one at a time.
    - a. Unwrap the plastic cap for the control and set the opening side down on top of the foil until the foil has been quickly lifted off the plastic bottle mouth; set the cap on the bottle mouth and quickly screw down.
    - b. Unwrap the glass stoppers by first unwrapping the "handle" end of the stopper so it may be held in one hand while the other hand quickly tears off the foil from the stopper end; then lift the foil off the mouth of the glass collection vessel; quickly place the stopper in the collection vessel.

7. Rinse the probe with solvent (acetone) from a wash bottle and capture the rinse in a used mixing vessel.
    - a. Pour the rinse into the toxic waste container in the hood.
    - b. Repeat the probe rinse-capture operations until the solvent dripping from the probe is clear.
    - c. Rinse the probe with clean distilled water by mixing a fresh portion of distilled water for 2 to 3 minutes in a clean 100 or 250 ml mixing vessel at SPEED 6.

8. Rinse the other mixing vessels used for emulsion preparation with solvent and pour the rinse into the waste container in the hood.

9. Place the dirty glassware in the sink for washing.

10. Remove the probe from the mixer and clean it immediately.

11. Make and affix paper labels to each container with the sequential preparation number assigned from the project logbook, prep. type, component concentrations, prep. person, and prep. date.

12. Deliver the emulsions and control to the materials users.

PREPARATION OF BENZO(a)PYRENE-Fe_2O_3 POWDER

STARTING MATERIALS (see RAW MATERIALS list, p. 11 & 12)

Benzo(a)pyrene: one lot for both phases
Iron Oxide: synthetic hematite
Laboratory Distilled Water
Reagent Grade Acetone
Crushed Ice

FINAL POWDER COMPOSITION

1:1 by mass, benzo(a)pyrene:iron oxide

PREPARATION SCHEDULE

Prepare fresh for each phase of the experiment

SAMPLE MASS REQUIREMENTS

Deliver 6.5 grams for each phase of the experiment; split each delivery into two containers

GLASSWARE, EQUIPMENT REQUIREMENTS

4000 ml glass beaker
400 ml glass beaker
glass stirring rod
2-liter filtration flask with rubber tubing
11.0 cm porcelain buchner funnel fitted with rubber stopper
11.0 cm Whatman No. 40 filter circles
2-gallon plastic bucket
9" x 9" magnetic stirrer plate
3" magnetic stirring bar
plastic wash bottles
hot plate
12 cm glass petri dish (top or bottom half)
2 5-dram amber vials
1 1-dram amber vial

PREPARATION OF BENZO(a)PYRENE-Fe_2O_3 POWDER (continued)

PREPARATION OF THE Fe_2O_3 NUCLEATING BATH

1. Fill the 4000 ml beaker with 3200 of laboratory distilled water and place it in the plastic bucket.

2. Pack crushed ice around the beaker in the bucket.

3. Put the stirring bar in the beaker and place the bucket on the magnetic stirrer; set the stirrer at SPEED 7.

4. Weigh out 3.5 g Fe_2O_3 into a foil weighing pan on the Torsion balance in 3F1-1,2 (see SOP posted for this balance).

5. Wet the Fe_2O_3 in the weighing pan with 5-10 ml of isopropyl alcohol; with a wash bottle filled with laboratory distilled water, rinse the Fe_2O_3-isopropanol from the foil pan into the vortex of the water in the 4000 ml beaker on the magnetic stirrer.

6. Mix the Fe_2O_3 in the water on the magnetic stirrer for 2 to 3 hours until the water reaches 4°C; repack as necessary with ice.

PREPARATION OF THE BENZO(a)PYRENE-ACETONE SOLUTION

1. Place the 400 ml beaker, a plastic wash bottle filled with reagent grade acetone, an acetone-cleaned foil weighing pan, and the bottle of benzo(a)pyrene into the glove box adjacent to hood no. 97 (in room 3F1-1,2). Use the isolation chamber entry port on the side to enter the glove box.

2. Weigh 3.5 g + 10% of benzo(a)pyrene into an acetone-cleaned foil weighing pan. Use the Torsion balance in the glove box adjacent to hood no. 97.

PREPARATION OF BENZO(a)PYRENE-Fe_2O_3 POWDER (continued)

3. Wet the benzo(a)pyrene in the foil pan with reagent grade acetone; then carefully rinse the benzo(a)pyrene into the 400 ml beaker with more acetone dispensed from a wash bottle.

4. Remove the beaker containing the benzo(a)pyrene and acetone from the glove box through the side entry isolation chamber.

5. Fill the beaker to the 300 ml mark with reagent grade acetone.

6. Gently heat the beaker on the hot plate on the left side of hood no. 97 (set the hot plate to 300°F on the dial) until all the benzo(a)pyrene is dissolved.

   Note: Frequent swirling and break-up of the benzo(a)pyrene lumps with the glass stirring rod will be necessary in order to get all the material in solution. Make sure benzo(a)pyrene that has crystallized onto the stirring rod and the walls of the beaker is rinsed down and redissolved.

NUCLEATION OF THE BENZO(a)PYRENE

1. Once the water suspension containing the iron oxide has reached 4°C and the benzo(a)pyrene solution has been prepared, set the magnetic stirrer at SPEED 7 and insure that a good vortex is present.

2. Slowly pour the hot acetone-benzo(a)pyrene into the vortex; running the solution down a stirring rod held deep within the vortex is recommended. As the benzo(a)pyrene solution cools, some of the benzo(a)pyrene will begin to crystallize out of solution. Therefore, it is necessary to return the solution to the hot plate for reheating after each 100 ml has been poured into the Fe_2O_3 suspension. The benzo(a)pyrene crystallized on the lip of the solution beaker and on the stirring rod must also be redissolved during each reheating.

PREPARATION OF BENZO(a)PYRENE-Fe_2O_3 POWDER (continued)

Note: No large, already formed crystals of benzo(a)pyrene must be poured into the Fe_2O_3 suspension from the acetone solution beaker.

3. Once all the benzo(a)pyrene solution has been added to the Fe_2O_3 suspension, slow the magnetic stirrer to SPEED 5 and continue stirring for one-half hour more.

4. The suspension will be a murky yellow color immediately after addition of benzo(a)pyrene-acetone solution, but will become clear (except for the red iron oxide tinting) after the additional stirring time. If a milky white to yellow coloration remains in the nucleating bath after the final stirring time, the benzo(a)pyrene was added too quickly and the benzo(a)pyrene has not properly precipitated onto the iron oxide.

RECOVERY OF THE BENZO(a)PYRENE-IRON OXIDE POWDER

1. Turn the magnetic stirrer off and remove the beaker from the ice bath. Remove the stirrer bar with a retriever and rinse it thoroughly with distilled water.

2. Set up the filtration apparatus.
   a. Connect the filtration flask side arm to the water faucet aspirator on the left side of hood no. 97 with rubber tubing.
   b. Insert the buchner funnel stopper in the neck of the filtration flask.
   c. Place one circle of filter paper in the buchner funnel, wet it with distilled water, and turn on the water flow to activate the aspirator.

PREPARATION OF BENZO(a)PYRENE-Fe_2O_3 POWDER (continued)

3. With the aspirator operating, carefully pour the benzo(a)pyrene-iron oxide-containing suspension into the buchner funnel until the funnel is full. Refill the funnel with suspension as necessary.

4. Empty the filtration flask before it overflows and while 0.25 to 0.5 inches of suspension are present in the buchner funnel.

5. Continue the filtration until all the suspension has been drained from the beaker. Thoroughly rinse the beaker with distilled water to remove remaining particles and drain these rinses into the buchner funnel.

6. Once all the suspension liquid has drained from the buchner funnel, rinse the captured particles with 10-20 mls of distilled water.

7. Leave the aspirator on until the filter cake of particles has sufficiently dried to start cracking (2 to 3 minutes after the last drops of water have dripped out).

8. Remove the filter paper containing the filter cake from the buchner funnel with the aid of a spatula and place in one side of a 12 cm glass petri dish.

9. Place the petri dish containing the filter cake in a desiccator in hood no. 98 for drying under nitrogen for 48 hours.
    a. Connect the desiccator to the dry nitrogen cylinder regulated air stream.
    b. Open the stopcock in the lid of the desiccator.
    c. Turn on the nitrogen stream at a delivery pressure of 10-15 psi.
    d. Check to insure that there is nitrogen exiting from the desiccator.

DELIVERY OF THE BP-Fe_2O_3 POWDER

1. Weigh the amber vials on the laboratory triple-beam balance and record the tare weights in the logbook.

2. Place the amber vials and a 10" x 10" square of aluminum foil in the glove box.

3. After the 48-hour drying period, turn off the nitrogen and remove the filter cake from the desiccator to the glove box. Enter the glove box from the side entry isolation chamber.

4. With a spatula, scrape the filter cake from the filter paper into the petri dish and discard the paper as toxic waste.

5. Break up the agglomerated benzo(a)pyrene-iron oxide mixture into a fine powder with the spatula.

6. Pour out the powdered BP-Fe_2O_3 mixture onto the square of aluminum foil, mix it thoroughly, and then equally divide the dry powder between the two 5-dram vials.

7. Remove one spatula-full of the dry powder from each 5-dram vial and place them in the 1-dram vial for a laboratory retain sample.

8. Seal the vials and carefully wipe them clean.

9. Remove the vials from the glove box through the side entry isolation chamber.

10. Reweigh the vials and record the final vial + sample weights in the logbook.

PREPARATION OF BENZO(a)PYRENE-Fe_2O_3 POWDER (continued)

11. Label the vials with the prep. number, prep. type, quantity of material, prep. person and prep. date.

12. Deliver the two 5-dram vials to the low temperature freezer (no. 4) in CRB 1E5-2 and leave the 1-dram vial in the refrigerator freezer of CRB 3F1-1,2.

APPENDIX B

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

B.1 First Replicate

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
SKIN/SUBCUTIS																											
Edema, diffuse/focal	6/99	----	4/49	4/49	5/49	6/50	3/50	4/48	2/24	6/49	3/49	7/48	----	----	2/48	6/49	3/24	6/49	3/47	----	----	2/48	6/49	2/49	----	3/49	
Abscess	15/99	3/49	9/49	9/49	10/49	7/50	10/50	4/48	1/24	4/49	11/49	4/48	5/25	6/49	9/48	10/49	6/24	14/49	10/47	11/48	----	3/48	9/49	5/49	1/25	10/49	
Mass	----	1/49	----	----	----	----	1/50	----	----	----	----	2/48	----	----	1/48	----	----	2/49	1/47	3/48	----	2/48	1/49	----	----	----	
Ulcer	1/99	----	1/49	----	----	----	----	----	----	----	2/49	1/48	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	
Exudative	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	
Necrosis	1/99	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Hair loss	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/48	----	1/24	----	----	----	----	----	1/49	----	----	----	
Red, diffuse/focal	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	
Green	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Yellow	----	----	----	----	1/49	----	1/50	----	----	----	----	----	----	----	1/48	1/49	1/24	----	----	----	----	----	----	1/49	----	----	
Thickened	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Crusty/scaly/dry/flaky	1/99	----	----	----	----	----	----	----	----	----	----	----	----	1/49	2/48	----	1/24	----	----	----	----	2/48	----	1/49	1/25	----	
Lesion	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	1/49	
TOTAL HAMSTERS WITH LESIONS	23/99	5/49	15/49	13/49	15/49	13/50	14/50	8/48	3/24	10/49	16/49	12/48	5/25	8/49	16/48	17/49	11/24	21/49	14/47	14/48	0/24	8/48	17/49	9/49	2/25	14/49	
MANDIBULAR SALIVARY GLAND																											
Enlarged	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Tan	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	
Mass	1/99	----	----	----	----	1/50	1/50	----	----	----	----	----	----	----	----	----	1/24	----	1/46	----	----	----	----	----	----	----	
Nodules	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Cyst(s)	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	
Necrosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	1/99	0/49	0/48	0/49	0/49	1/50	1/50	0/47	0/23	2/49	0/49	0/48	0/25	0/48	0/48	2/49	1/24	0/49	1/46	0/48	0/24	1/47	0/49	0/48	1/25	0/49	
MANDIBULAR LYMPH NODES																											
Enlarged	3/99	1/49	2/48	1/49	----	----	1/50	1/48	1/23	3/49	----	----	----	----	----	1/49	1/24	----	1/46	----	1/24	1/47	2/49	----	----	----	
Mottled red	3/99	1/49	2/48	1/49	----	----	1/50	1/48	----	2/49	----	1/48	----	----	----	----	2/24	----	1/46	----	1/24	1/47	2/49	----	1/25	----	
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	1/50	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Soft	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/46	----	----	----	----	----	----	----	
Necrosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	3/99	1/49	2/48	1/49	0/49	0/50	1/50	1/48	1/23	3/49	0/49	1/48	0/25	0/49	0/49	1/49	2/24	0/49	2/46	0/48	1/24	1/47	2/49	0/48	1/25	0/49	
MAMMARY GLAND																											
Discolored	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	1/48	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/49	0/49	1/49	0/48	0/50	0/50	1/48	0/24	0/49	1/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/47	0/48	0/24	0/48	0/49	0/49	0/25	0/49	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
STERNUM																										
Mottled black	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Inverted	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Lesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/48	0/49	1/49	1/50	0/50	0/48	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/47	0/48	0/24	0/48	0/49	0/49	0/25	1/49	
EOSTOCHONDRAL																										
Nodule	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/48	1/49	0/49	0/50	0/50	0/48	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/47	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
THYMUS																										
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	
Mass	1/99	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	1/99	0/50	0/49	0/49	0/49	0/50	0/50	0/48	0/24	0/48	1/49	0/48	0/25	0/48	0/49	0/49	0/24	0/49	1/48	0/48	0/24	1/48	0/49	0/49	0/25	0/49	
THYROIDS																										
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Enlarged	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	1/48	----	----	----	----	1/49	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	1/49	0/49	0/50	0/50	0/48	0/24	0/48	1/49	0/48	0/25	0/47	0/49	0/49	0/24	0/49	1/48	0/48	0/24	0/48	0/49	1/49	0/25	0/49	
PARATHYROID																										
Mass	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/48	0/24	0/48	1/49	0/48	1/25	0/47	0/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
HEART																										
Mottled black	----	----	1/49	----	----	2/50	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Tan/yellow	1/99	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	
Enlarged	----	----	----	----	2/49	1/50	----	----	----	----	1/49	----	----	----	1/49	----	----	----	1/48	1/47	----	1/48	----	----	----	----	
Small	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	1/48	1/47	----	1/48	----	----	----	----	
Cyst	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass/growth	1/99	----	----	----	----	----	----	----	----	----	1/49	----	----	----	1/49	----	----	----	----	----	1/24	----	----	----	----	1/49	
Nodules	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	2/49	----	----	----	----	1/24	----	----	----	1/25	----	
Thrombosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/47	----	----	----	----	----	----	
Adhesion	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	2/99	0/50	1/49	0/49	2/49	3/50	1/50	0/49	0/24	0/48	2/49	0/48	0/25	1/48	3/49	3/49	0/23	0/49	2/48	3/47	1/24	1/48	0/49	0/49	1/25	1/49	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
HEART (AURICLES)																										
Enlarged	17/99	6/50	6/49	8/49	4/49	11/50	6/50	9/49	4/24	6/48	7/49	9/48	3/25	9/48	10/49	6/49	4/23	5/49	7/48	3/47	5/24	5/48	8/49	8/49	4/25	6/49	
Firm	14/99	3/50	5/49	8/49	5/49	8/50	5/50	8/49	4/24	4/48	7/49	6/48	3/25	7/48	10/49	4/49	3/23	7/49	6/48	3/47	5/24	5/48	6/49	7/49	2/25	4/49	
Tan	1/99	1/50	1/49	----	2/49	2/50	1/50	3/49	1/24	----	2/49	4/48	3/25	1/48	2/49	1/49	1/23	3/49	2/48	----	----	1/48	1/49	4/49	----	1/49	
Mottled red	----	1/50	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	
Mottled white	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	1/24	----	----	----	2/25	----	
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	17/99	6/50	6/49	8/49	5/49	11/50	6/50	9/49	4/24	6/48	7/49	10/48	3/25	9/48	11/49	6/49	4/23	7/49	7/48	3/47	5/24	5/48	8/49	8/49	4/25	6/49	
ESOPHAGUS																										
Mottled red	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Contained black material	----	----	----	----	----	----	----	----	----	----	----	----	----	2/47	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/98	0/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	1/48	0/49	0/48	0/25	2/47	0/48	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
TRACHEA																										
Contained black material	----	19/50	14/49	5/49	----	22/50	11/50	16/49	----	----	----	----	1/25	3/47	1/48	----	1/24	1/49	----	----	----	----	----	----	----	----	
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	
Contained red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/98	19/50	14/49	5/49	0/49	22/50	11/50	16/49	0/24	0/48	0/49	0/48	1/25	3/47	1/48	0/49	1/24	1/49	1/48	0/47	0/24	0/48	0/49	0/49	0/25	0/49	
LUNGS																										
Mottled brown	5/99	3/50	3/49	1/49	----	----	----	1/49	4/24	4/48	6/49	3/48	6/25	15/48	19/49	5/49	6/24	4/49	5/48	5/47	5/24	5/48	10/49	2/49	3/25	2/49	
Mottled black	3/99	50/50	43/49	45/49	3/49	49/50	41/50	36/49	5/24	10/48	8/49	5/48	12/25	11/48	15/49	14/49	7/24	15/49	5/48	12/47	6/24	7/48	6/49	5/49	9/25	9/49	
Mottled red	51/99	6/50	16/49	25/49	29/49	11/50	15/50	19/49	12/24	26/48	30/49	30/48	11/25	21/48	25/49	28/49	11/24	33/49	25/48	25/47	18/24	21/48	26/49	27/49	16/25	26/49	
Mottled grey	1/99	2/50	1/49	----	----	----	----	----	----	----	----	2/48	----	----	----	----	----	1/49	2/48	1/47	----	----	----	----	----	5/49	
Dark spots	1/99	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/25	2/49	
Mottled/spotted	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	1/49	----	----	----	----	----	----	----	1/49	
Nodule	----	----	----	----	----	2/50	1/50	1/49	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	1/49	----	----	1/49	----	----	----	----	2/49	----	1/49	1/48	----	----	----	----	----	1/25	----	
Cyst(s)	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	
Contained red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	1/49	----	----	----	----	----	----	----	----	
Enlarged, focal/diffuse	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	
Adhesion	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan, focal/multifocal	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	
White foci	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/49	
TOTAL HAMSTERS WITH LESIONS	55/99	50/50	49/49	47/49	31/49	49/50	46/50	44/49	18/24	34/48	40/49	38/48	24/25	44/48	44/49	43/49	21/24	43/49	33/48	39/47	23/24	35/48	36/49	31/49	21/25	38/49	
LARYNX																										
Mottled black/contained black material	----	2/50	----	----	----	1/50	1/50	1/49	----	----	----	----	1/25	----	----	----	----	1/49	----	----	----	----	----	----	----	----	
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	2/50	0/49	0/49	0/49	1/50	1/50	1/49	0/24	0/49	0/49	0/48	1/25	0/47	0/49	0/49	0/24	1/49	0/48	0/48	0/24	0/48	0/49	0/48	0/25	0/49	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe$_2$O$_3$ 5 mg	DP:Fe$_2$O$_3$ 2.5 mg	DP:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	DE:Fe$_2$O$_3$ 5 mg	DE:Fe$_2$O$_3$ 2.5 mg	DE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	COE:Fe$_2$O$_3$ 5 mg	COE:Fe$_2$O$_3$ 2.5 mg	COE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	CSC:Fe$_2$O$_3$ 5 mg	CSC:Fe$_2$O$_3$ 2.5 mg	CSC:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	RTE:Fe$_2$O$_3$ 5 mg	RTE:Fe$_2$O$_3$ 2.5 mg	RTE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	BP:Fe$_2$O$_3$ 2 mg	Gelatin Saline 0.5%
RESPIRATORY LYMPH NODES																											
Mottled black/contained black material	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	
Enlarged	----	----	----	----	----	----	1/50	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled red	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	1/50	0/49	0/24	0/49	1/49	1/48	1/25	0/47	0/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
LIVER																											
Cyst(s)	17/98	14/50	9/47	10/49	8/49	12/50	13/50	13/48	5/24	11/48	7/49	9/48	7/25	6/48	8/49	9/49	2/24	10/49	8/47	3/48	8/24	10/47	9/49	8/49	5/24	8/49	
Tan, diffuse/focal/ multifocal	2/98	1/50	1/47	4/49	3/49	2/50	2/50	1/48	2/24	2/48	1/49	2/48	1/25	----	4/49	2/49	1/24	2/49	2/47	3/48	3/24	2/47	----	4/49	----	2/49	
Pitted, granular	5/98	----	2/47	3/49	2/49	5/50	2/50	2/48	2/24	1/48	3/49	1/48	----	2/48	4/49	2/49	2/24	2/49	1/47	6/48	1/24	1/47	1/49	2/49	----	1/49	
Enlarged/thickened	6/98	1/50	5/47	6/49	5/49	1/50	2/50	3/48	1/24	1/48	3/49	5/48	----	----	7/49	3/49	3/24	1/49	2/47	1/48	----	3/47	2/49	4/49	----	1/49	
Soft	----	----	----	----	1/49	----	----	----	----	1/48	1/49	----	----	----	----	2/49	----	----	----	1/48	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	1/48	----	1/48	----	----	----	----	----	1/49	----	2/48	----	----	1/49	----	----	1/49	
Mottled red	8/98	2/50	3/47	4/49	7/49	5/50	1/50	1/48	2/24	2/48	3/49	6/48	1/25	3/48	6/49	2/49	3/24	2/49	2/47	2/48	2/24	3/47	1/49	3/49	----	3/49	
Mottled brown	2/98	1/50	1/47	2/49	2/49	2/50	1/50	----	1/24	----	3/49	----	1/25	1/48	----	1/49	----	----	----	----	----	2/47	----	----	1/24	----	
Dark brown, diffuse/ multifocal	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	1/24	----	----	----	----	----	
Mottled black	2/98	----	1/47	1/49	1/49	----	1/50	2/48	----	1/48	----	1/48	----	----	2/49	----	1/24	2/49	2/47	1/48	1/24	1/47	2/49	----	----	1/49	
Spotted/multiple foci/ discolored	----	----	----	----	----	----	----	----	----	----	1/49	1/48	----	----	----	----	----	1/49	----	----	----	----	----	----	----	1/49	
Nodule	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	1/49	----	----	----	----	----	----	1/24	----	
Mass	1/98	----	----	2/49	1/49	----	----	1/48	----	----	----	----	1/25	----	1/49	----	----	----	----	----	----	----	2/49	----	1/24	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	1/49	
Adhesion	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Green foci	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	28/98	15/50	14/47	18/49	17/49	19/50	15/50	15/48	9/24	17/48	15/49	14/48	8/25	10/48	19/49	15/49	5/24	15/49	14/47	10/48	10/24	16/47	12/49	16/49	7/24	15/49	
GALL BLADDER																											
Distended/enlarged/thickened	1/97	1/50	----	----	----	----	1/50	----	----	----	----	1/48	----	----	----	1/49	----	1/49	----	1/48	----	1/47	----	----	----	----	
Contained fluid (black/ yellow/red)	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	2/49	1/47	----	----	----	----	----	1/24	1/49	
Small	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Black	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Aplastic	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	
TOTAL HAMSTERS WITH LESIONS	1/97	1/50	1/47	0/49	2/49	0/50	1/50	0/48	0/24	0/48	0/49	1/48	1/25	0/48	0/49	1/49	0/24	2/49	1/47	1/48	0/24	1/47	0/49	1/49	1/24	1/49	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe$_2$O$_3$ 5 mg	DP:Fe$_2$O$_3$ 2.5 mg	DP:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	DE:Fe$_2$O$_3$ 5 mg	DE:Fe$_2$O$_3$ 2.5 mg	DE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	COE:Fe$_2$O$_3$ 5 mg	COE:Fe$_2$O$_3$ 2.5 mg	COE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	CSC:Fe$_2$O$_3$ 5 mg	CSC:Fe$_2$O$_3$ 2.5 mg	CSC:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	RTE:Fe$_2$O$_3$ 5 mg	RTE:Fe$_2$O$_3$ 2.5 mg	RTE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	BP:Fe$_2$O$_3$ 2 mg	Gelatin Saline 0.5%
ADRENAL GLANDS																											
Tan/yellow	27/98	19/49	14/47	19/47	13/48	25/50	17/50	15/48	9/24	18/48	13/49	12/48	9/25	14/48	14/48	13/49	4/24	12/49	8/47	11/48	6/24	13/47	13/49	13/49	2/24	11/48	
Pitted	1/98	----	----	----	1/48	1/50	1/50	1/48	----	----	----	----	----	2/48	1/48	----	----	----	----	----	----	1/47	----	1/49	----	1/48	
Enlarged	9/98	11/49	6/47	7/47	5/48	14/50	4/50	9/48	4/24	7/48	7/49	5/48	1/25	8/48	7/48	6/49	2/24	5/49	3/47	6/48	2/24	8/47	6/49	7/49	----	4/48	
Red, diffuse/multifocal	1/98	----	----	----	----	----	----	1/48	----	----	----	----	----	2/48	----	1/49	----	----	----	1/48	----	----	----	1/49	----	2/48	
Black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	1/48	----	----	----	----	----	----	
Brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	
Grey/white	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Small	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	
Firm	1/98	1/49	----	1/47	1/48	----	----	----	1/24	1/48	----	----	----	----	----	1/49	----	----	----	----	----	----	1/49	----	----	----	
Mass	----	----	1/47	----	1/48	----	1/50	----	----	----	----	----	----	----	1/48	1/49	----	----	4/47	----	1/24	1/47	----	----	----	----	
Adhesions	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Aplastic	1/98	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Lobular	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Necrotic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	28/98	20/49	14/47	20/47	14/48	26/50	19/50	16/48	10/24	18/48	15/49	12/48	9/25	16/48	16/48	14/49	5/24	15/49	12/47	12/48	7/24	15/47	13/49	15/49	2/24	11/48	
SPLEEN																											
Enlarged	9/97	5/49	3/47	5/47	9/48	5/49	6/49	6/48	6/24	4/47	4/49	6/48	1/24	6/48	4/49	8/48	3/24	2/49	3/47	10/48	1/24	5/47	7/48	7/48	3/24	7/47	
Small	1/97	1/49	1/47	1/47	----	1/49	----	----	----	----	----	----	1/24	3/48	----	----	----	1/49	2/47	1/48	----	1/47	----	----	----	----	
Red, diffuse/focal	1/97	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	1/48	----	1/47	----	----	----	----	
Nodule	----	1/49	----	----	1/48	----	----	----	1/24	----	----	----	----	----	----	1/48	1/24	----	----	----	----	1/47	----	1/48	----	2/47	
Mass	----	----	----	1/47	----	1/49	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	1/47	1/48	----	----	1/47	
Pitted/granular	1/97	----	----	----	----	2/49	----	----	1/24	----	2/49	----	----	1/48	2/49	1/48	----	1/49	1/47	1/48	----	----	----	1/48	----	----	
Ruptured/divided	----	----	1/47	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Accessory	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled black	1/97	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	
Tan, focal/multifocal	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	1/48	----	----	
Grey/white foci	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	
Cystic/transparent foci	----	----	----	----	----	----	1/49	----	----	----	----	1/48	----	----	----	----	1/24	1/49	----	----	----	1/47	----	1/48	----	----	
Blood clots	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	12/97	7/49	5/47	7/47	10/48	9/49	7/49	7/48	6/24	4/47	4/49	7/48	4/24	11/48	5/49	9/48	4/24	5/49	6/47	13/48	1/24	10/47	8/48	9/48	3/24	10/47	
KIDNEYS																											
Tan/pale/grey	24/98	11/50	12/47	13/47	9/48	17/50	14/50	14/48	6/24	15/48	9/49	13/48	8/25	15/48	16/48	18/49	6/24	11/49	17/47	9/48	7/24	8/47	11/49	12/49	4/24	7/48	
Pitted/granular	24/98	17/50	11/47	15/47	14/48	15/50	14/50	19/48	8/24	15/48	10/49	13/48	9/25	16/48	19/48	19/49	7/24	14/49	19/47	8/48	8/24	15/47	10/49	14/49	6/24	15/48	
Enlarged	----	----	----	1/47	2/48	----	1/50	1/48	----	----	1/49	2/48	----	----	----	1/49	2/24	2/49	----	----	----	----	1/49	1/49	----	----	
Small	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	1/49	----	----	----	
Red, diffuse/focal	----	----	----	----	----	1/50	----	----	----	1/48	----	----	----	----	1/48	----	----	----	1/47	----	----	1/47	1/49	----	----	----	
Mottled black	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	1/47	----	----	----	----	
Mottled brown/dark brown	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	1/48	1/24	----	----	----	----	----	
Mass	----	----	----	----	1/48	----	2/50	----	----	----	----	----	----	----	1/48	1/49	----	1/49	2/47	----	2/24	1/47	1/49	----	----	----	
Nodules	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Lobular	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
KIDNEYS (contd)																											
Soft	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	1/98	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Cyst(s)	1/98	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Covered with red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	32/98	18/50	15/47	18/47	14/48	20/50	20/50	21/48	8/24	19/48	12/49	16/48	10/25	20/48	23/48	22/49	9/24	19/49	21/47	11/48	12/24	17/47	17/49	17/49	6/24	16/48	
URINARY BLADDER																											
Contained calculi	2/96	1/49	----	----	1/49	----	----	1/48	----	----	----	----	1/24	----	1/49	----	----	1/49	----	----	----	----	1/49	1/49	----	----	
Distended	----	----	----	----	1/49	----	----	----	----	----	----	----	1/24	----	----	----	1/24	----	1/46	----	----	----	----	1/49	----	----	
Thickened walls	----	----	----	----	2/49	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	1/47	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	
Small	1/96	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	1/49	----	----	----	1/47	1/49	----	----	----	
Contained fluid, red/ dark brown	1/96	----	----	----	1/49	----	----	----	1/24	----	----	----	----	----	----	----	----	----	----	2/48	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	4/96	1/49	0/49	1/47	5/49	1/50	0/50	1/48	1/24	0/48	0/48	1/47	2/24	0/48	1/49	0/49	1/24	2/49	1/46	3/48	0/23	1/47	2/49	2/49	0/24	1/49	
TESTES																											
Small/degenerated	33/97	18/49	20/48	20/47	21/49	19/50	22/50	18/48	10/23	16/48	24/49	16/47	10/24	15/48	21/49	25/49	10/24	25/49	21/46	24/48	9/24	19/47	20/49	19/49	8/24	18/49	
Aplastic	----	----	----	----	1/49	1/50	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Dark red	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	
Grey	----	----	1/48	1/47	1/49	1/50	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	
Dark brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Black	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	
Covered with red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	
Abscess/infected	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	1/49	----	----	----	----	2/24	----	----	1/49	----	1/49	
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	33/97	18/49	21/48	20/47	22/49	21/50	23/50	19/48	10/23	16/48	24/49	16/47	10/24	15/48	22/49	25/49	10/24	25/49	21/46	25/48	11/24	19/47	20/49	19/49	8/24	20/49	
EPIDIDYMIS																											
Small/degenerated	9/96	4/49	4/48	5/47	6/49	11/50	7/50	6/48	5/23	6/48	6/49	6/47	5/24	3/48	8/49	6/49	4/24	9/49	5/46	7/48	6/24	4/47	9/49	6/49	2/24	6/48	
Flaccid	----	1/49	----	1/47	2/49	1/50	1/50	1/48	----	4/48	----	1/47	----	1/48	1/49	----	2/24	2/49	2/46	4/48	----	----	----	----	----	1/48	
Aplastic	----	----	1/48	----	----	1/50	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess/infected	1/96	----	----	----	1/49	----	----	----	----	1/48	----	1/47	1/24	----	1/49	1/49	----	1/49	----	----	----	----	----	2/49	1/24	1/48	
Enlarged	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	1/49	----	----	----	1/46	----	----	----	2/49	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/46	----	----	----	1/49	----	----	----	
Black	1/96	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Cystic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	10/96	4/49	5/48	6/67	8/49	13/50	7/50	8/48	5/23	9/48	6/49	9/47	5/24	4/48	10/49	7/49	4/24	11/49	8/46	9/48	7/24	4/47	11/49	7/49	3/24	8/48	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
SEMINAL VESICLES																											
Small	9/96	3/49	5/48	4/47	3/49	6/50	5/50	3/48	4/24	5/48	5/49	4/47	3/24	2/48	6/49	6/49	3/24	8/49	4/45	3/48	3/23	3/47	8/49	5/49	2/24	7/48	
Flaccid	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/45	----	----	----	----	----	----	----	
Red	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	1/45	----	----	----	----	----	----	----	
Black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Yellow	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	
Contained fluid, red/yellow/ brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess/infected	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	
Aplastic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	
Adhesions	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	1/47	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	9/96	3/49	5/48	5/47	3/49	6/50	5/50	3/48	5/24	5/48	5/49	7/47	3/24	2/48	7/49	6/49	3/24	9/49	5/45	4/48	3/23	3/47	8/49	5/49	2/24	7/48	
PROSTATE																											
Small	1/96	----	1/49	----	1/49	---	1/50	----	2/24	----	----	1/47	----	----	----	----	----	1/49	----	1/48	----	----	2/48	----	----	1/49	
Mass	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Cystic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	1/96	0/49	1/49	1/47	1/49	0/50	1/50	0/48	2/24	0/48	0/49	1/47	0/24	0/28	0/49	0/49	0/24	1/49	0/46	1/48	0/23	0/47	2/48	0/49	0/24	1/49	
PANCREAS																											
Adhesion	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan/yellow	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Fatty infiltration	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Nodules	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/97	0/49	0/48	1/47	0/48	0/49	0/48	0/48	0/24	0/47	0/49	1/48	1/24	0/28	1/49	0/48	0/24	0/49	0/47	0/48	0/23	0/47	1/48	0/48	0/24	0/47	
STOMACH																											
Black foci, mucosa/serosa	----	1/49	1/48	1/47	----	3/49	----	2/48	----	2/48	1/49	2/48	----	----	2/49	2/49	1/24	1/48	3/47	2/48	3/24	4/47	1/48	----	----	----	
Contained material, red/ brown-green	1/96	----	----	1/47	2/49	1/49	----	----	1/24	1/48	2/49	2/48	----	1/48	2/49	1/49	----	----	----	----	----	----	----	1/48	----	1/46	
Distended/gas filled	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	----	2/48	----	----	----	----	----	----	
Tan/yellow	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	1/48	----	----	
Mottled red, mucosa/serosa	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/24	----	----	----	----	----	
Mottled brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	1/24	----	----	----	----	----	
Thickened	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	
Edematous	----	----	----	----	----	----	----	----	----	----	----	----	----	---	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	1/47	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	
Nodules	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Dark foci, mucosa/serosa	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3, 2 mg	Gelatin Saline 0.5%
STOMACH (contd)																											
Cyst(s)	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	1/96	1/49	1/48	3/47	3/49	5/49	0/48	2/48	2/24	3/48	3/49	4/48	1/25	1/48	4/49	3/49	1/24	1/48	3/47	5/48	5/24	4/47	3/48	2/48	0/24	1/46	
DUODENUM																											
Contained material/fluid (red, brown-green)	2/96	2/49	3/47	----	3/49	1/48	----	----	1/24	----	1/48	----	1/23	1/48	----	----	1/23	----	----	1/48	----	----	2/48	----	----	----	
Tan/yellow/white	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	1/49	----	1/48	----	----	----	----	----	1/49	----	----	
Nodules	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	1/23	----	----	----	----	----	----	----	----	----	
Herniated	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Distended/gas filled/enlarged	----	----	----	----	----	----	----	----	1/24	----	----	1/48	----	----	----	----	----	----	----	3/48	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	2/96	2/49	3/47	2/47	3/49	2/48	0/48	1/48	2/24	0/48	1/48	1/48	1/23	1/48	1/49	1/49	2/23	1/48	0/47	4/48	0/24	0/47	2/48	1/49	0/24	0/46	
JEJUNUM																											
Contained material/fluid (red, brown-green)	2/96	2/49	3/47	----	4/49	2/48	1/48	----	1/24	----	1/48	----	1/23	1/48	----	----	1/23	----	----	1/48	----	----	2/48	----	----	----	
Distended/gas filled	----	----	----	----	----	----	----	----	1/24	----	----	1/48	----	----	----	----	----	----	----	3/48	----	----	----	----	----	----	
Tan/yellow/white	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	1/49	----	1/48	----	----	----	----	----	1/49	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/23	----	----	----	----	----	----	----	----	----	
Herniated	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Intussusception	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Nodules	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	2/96	2/49	3/47	2/47	4/49	2/48	1/48	1/48	2/24	0/48	1/48	1/48	1/23	1/48	0/49	1/49	2/23	1/48	0/47	4/48	0/24	0/47	2/48	1/49	1/24	0/46	
ILEUM																											
Contained material/fluid (red, brown-green)	2/96	2/49	3/47	----	4/49	2/48	----	----	1/23	----	1/48	----	1/23	1/48	----	----	1/23	----	----	1/48	----	----	2/48	----	----	----	
Distended/gas filled	----	----	----	----	----	----	----	----	1/23	----	----	1/48	----	----	----	----	----	----	----	3/48	----	----	----	----	----	----	
Tan/yellow/white	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	1/49	----	1/48	----	----	----	----	----	1/49	----	----	
Green	1/96	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Herniated	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/23	----	----	----	----	----	----	----	----	----	
Adhesion	1/96	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Intussusception	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	3/96	2/49	3/47	1/47	4/49	2/48	0/48	1/48	2/23	0/48	1/48	1/48	1/23	1/48	0/49	1/49	2/23	2/48	0/47	4/48	0/24	0/47	2/48	1/49	0/24	0/46	
CECUM																											
Contained material/fluid (red, brown-green)	2/96	1/49	1/48	----	2/49	2/48	----	----	----	1/48	1/48	2/48	----	2/48	----	----	2/23	1/48	1/47	3/48	----	2/47	----	----	----	----	
Distended/gas filled/enlarged	1/96	----	----	1/47	----	----	----	----	1/23	----	----	1/48	----	----	----	----	----	----	----	3/48	----	----	----	----	----	----	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
CECUM (contd)																											
Nodule	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	1/96	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	1/23	----	----	----	----	1/47	----	----	----	----	
Abscess	1/96	1/49	1/48	1/47	----	1/48	1/48	----	1/23	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan/yellow	----	----	----	2/47	1/49	----	----	----	----	----	----	----	----	----	----	1/49	----	1/48	----	----	----	----	----	1/49	----	----	
Herniated	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Red, diffuse/multifocal	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Grey	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Thickened	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	4/96	2/49	2/48	3/47	3/49	4/48	1/48	1/48	2/23	2/48	2/48	3/48	0/23	2/48	0/49	1/49	3/23	2/48	1/47	6/48	0/24	3/47	0/48	1/49	0/24	0/46	
COLON																											
Contained material/fluid (red, brown-green)	1/96	1/49	----	----	3/49	1/48	----	----	----	----	----	----	----	----	----	----	1/23	----	----	----	----	----	----	----	----	----	
Distended, gas filled	----	----	----	----	----	----	----	----	1/23	----	----	----	----	----	----	----	----	----	----	2/48	----	----	----	----	----	----	
Abscess	1/96	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan/yellow/white	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	2/49	----	1/48	----	----	----	----	----	1/49	----	----	
Obstruction	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	1/48	----	----	----	----	----	----	1/23	----	1/49	----	1/23	----	----	----	----	----	----	----	----	----	
Nodule	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	1/23	1/48	----	----	----	----	----	----	----	----	
Green, diffuse/focal	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Intussusception	----	----	----	----	----	----	----	----	----	1/48	----	----	----	1/48	----	----	1/23	1/48	----	----	1/24	2/47	----	----	----	----	
Empty	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Herniated	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	
Protruding	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	2/96	1/49	0/48	1/47	3/49	3/48	0/48	0/48	1/23	1/48	0/48	0/48	1/23	1/48	1/49	2/49	3/23	3/48	0/47	2/48	1/24	2/47	0/48	1/49	0/24	0/46	
RECTUM																											
Contained material/fluid (red, brown-green)	1/96	1/49	----	----	1/49	2/48	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	
Herniated	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	
Prolapse	----	----	----	----	----	----	----	----	----	1/48	----	----	----	1/48	----	----	----	----	1/46	----	----	2/47	----	----	----	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/46	
Tan/yellow/white	----	----	----	1/47	----	----	----	----	----	----	----	----	----	----	----	1/49	----	1/48	----	----	----	----	----	1/49	----	----	
Distended/gas filled	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/48	----	----	----	----	----	----	
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	1/96	1/49	0/48	1/47	1/49	2/48	0/48	0/48	0/23	1/48	0/48	0/48	0/23	1/48	0/49	1/49	2/24	2/48	1/46	2/48	0/24	2/47	0/48	1/49	0/24	1/46	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
MESENTERIC LYMPH NODES																											
Tan/pale/yellow	2/96	2/49	1/47	3/47	----	2/50	1/49	2/48	1/23	----	1/48	2/48	2/23	2/48	----	----	1/24	----	1/47	----	----	2/47	1/48	----	3/24	----	
Enlarged	13/96	3/49	6/47	6/47	5/49	3/50	2/49	5/48	3/23	5/48	1/48	3/48	1/23	4/48	2/49	1/49	2/24	2/49	5/47	----	----	6/47	2/48	2/48	3/24	3/46	
Mottled red/dark red	2/96	----	----	----	1/49	----	----	----	1/23	----	----	2/48	----	----	----	----	----	----	2/47	----	----	1/47	----	----	----	1/46	
Abscess	----	----	----	2/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled black/contained black material	----	----	----	----	2/49	----	----	1/48	1/23	----	----	----	----	----	----	----	----	----	----	2/48	----	1/47	----	----	----	----	
Dark color	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/49	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	2/48	----	----	----	----	1/24	----	----	----	----	----	1/48	----	----	2/46	
Brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	
Firm	1/96	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Soft	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Cyst(s)	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	13/96	3/49	6/47	8/47	7/49	3/50	2/49	6/48	3/23	5/48	1/48	6/48	2/23	4/48	2/49	1/49	3/24	2/49	5/47	2/48	0/24	6/47	3/48	3/49	3/24	4/46	
SKELETAL MUSCLE																											
Brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/48	0/49	0/50	0/50	0/48	0/24	0/48	0/49	0/48	0/25	0/48	0/49	0/49	0/24	0/49	0/47	0/48	0/24	0/47	0/49	0/49	0/25	0/49	
SCIATIC NERVE	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/48	0/49	0/50	0/50	0/48	0/24	0/48	0/49	0/48	0/24	0/49	0/49	0/49	0/24	0/49	0/47	0/48	0/24	0/47	0/48	0/49	0/25	0/49	
EYES																											
White/grey/brown/corneal opacity, focal, diffuse	2/98	1/50	----	1/49	2/48	1/50	----	----	----	----	----	----	----	1/49	1/49	----	----	----	----	----	1/24	----	2/49	1/48	----	3/49	
Small	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	1/49	----	----	----	----	----	----	----	1/49	----	----	----	
Crust formation	----	1/50	1/49	----	2/48	----	----	1/48	1/23	----	1/49	----	----	1/49	----	----	----	----	1/46	----	1/24	----	----	----	----	----	
Exudative	----	----	----	----	----	2/50	----	2/48	----	1/48	1/49	----	1/25	----	----	----	----	----	1/46	----	----	----	1/49	----	----	1/49	
Degenerated/missing	4/98	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	1/49	----	1/47	----	----	----	1/48	----	----	
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Discolored	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Protruding	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Hard	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Orbital Abscess	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	6/98	2/50	1/49	1/49	4/48	3/50	0/50	2/48	1/23	1/48	2/49	0/47	1/25	2/49	1/49	0/49	0/24	1/49	1/46	1/47	2/24	0/47	3/49	2/48	0/25	4/49	
EAR																											
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/48	0/50	0/50	0/48	0/23	0/48	0/48	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/46	0/48	0/24	0/47	0/49	0/48	0/25	0/49	
NASAL TURBINATES																											
Mass	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	2/49	----	----	----	----	----	----	----	----	----	----	
Contained red material	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/98	1/50	0/49	0/49	1/49	0/50	0/50	0/48	0/23	0/48	0/48	0/47	0/25	0/49	0/49	2/49	0/24	0/48	0/47	0/48	0/24	0/47	0/49	0/48	0/25	0/49	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
BRAIN																										
Mottled red	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Mottled brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	
Covered with red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Tan	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Blood clot	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Edematous	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/46	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/98	0/50	0/49	0/49	1/48	0/50	0/50	0/48	0/23	0/48	0/49	0/48	0/25	0/49	0/49	2/49	0/24	0/49	0/46	1/46	0/24	0/47	0/49	0/49	0/25	0/49	
PITUITARY GLAND																										
Dark red	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/98	0/50	0/49	0/49	0/48	0/50	0/50	1/48	0/23	0/48	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/47	0/46	0/24	0/47	0/49	0/48	0/25	0/49	
SPINAL CORD/COLUMN																										
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/98	0/50	0/49	0/49	0/49	0/50	0/50	0/48	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	1/24	0/49	0/47	0/47	0/24	0/47	0/49	0/49	0/25	0/49	
CHEEK POUCH																										
Mass	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	1/49	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/48	0/24	1/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/47	1/48	0/24	0/47	0/49	1/49	0/25	0/49	
THORACIC CAVITY																										
Contained fluid	----	1/50	----	----	1/49	1/50	1/50	1/49	----	----	----	1/48	----	1/49	2/49	----	1/24	2/49	----	----	1/24	----	1/49	2/49	1/25	----	
Contained red material/blood filled	----	----	----	----	1/49	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	
Mass	----	----	----	----	----	1/50	----	----	----	----	1/49	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	1/50	0/49	0/49	2/49	1/50	1/50	2/49	0/24	0/49	1/49	1/48	0/25	1/49	2/49	0/49	1/24	2/49	1/48	0/48	1/24	0/48	2/49	2/49	1/25	0/49	
ABDOMINAL CAVITY																										
Contained fluid	2/99	1/50	1/49	3/49	4/49	3/50	1/50	1/49	1/24	2/49	1/49	3/48	----	2/49	3/49	3/49	----	1/49	1/48	----	1/24	1/48	1/49	3/49	1/25	----	
Contained red material/blood filled	----	----	----	----	2/49	1/50	1/50	1/49	----	----	----	----	1/25	----	1/49	----	----	----	----	----	1/24	----	----	----	----	----	
Mass	1/99	----	----	1/49	----	1/50	----	----	----	----	1/49	----	----	----	----	----	2/24	----	----	----	----	----	----	----	----	----	
Abscess/contained green material	1/99	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Cyst(s)	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	4/99	1/50	1/49	3/49	6/49	4/50	2/50	2/49	1/24	2/49	2/49	3/48	1/25	2/49	4/49	3/49	2/24	1/49	1/48	0/48	2/24	1/48	1/49	3/49	1/25	0/48	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CDE:Fe_2O_3 5 mg	CDE:Fe_2O_3 2.5 mg	CDE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
PAW(S)																										
Swollen	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	
Red	1/99	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Grey	1/99	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	1/99	1/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	1/49	
MOUTH																										
Contained red material/ hemorrhage	----	1/50	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	1/50	1/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	1/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
PELVIC/LUMBAR LYMPH NODES																										
Enlarged	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/48	0/49	0/50	0/50	0/49	0/24	0/49	0/49	1/48	0/25	0/49	0/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
RENAL LYMPH NODES																										
Enlarged	----	----	----	----	----	----	1/50	----	1/24	1/49	----	----	----	----	----	----	1/24	----	1/48	----	----	----	----	----	----	----	
Red	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/48	0/49	0/50	1/50	0/49	1/24	1/49	0/49	0/48	0/25	0/49	0/49	0/49	1/24	0/49	1/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
MANDIBLE																										
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	1/48	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	2/49	0/49	0/24	0/49	0/48	1/48	0/24	0/48	0/49	0/49	0/25	0/49	
SKULL																										
Contained red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
AUXILIARY LYMPH NODES																										
Enlarged	----	----	----	----	----	----	1/50	----	----	----	----	1/48	----	----	----	----	1/24	----	----	----	----	----	----	1/49	----	----	
Red	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	
Tan	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Black	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	1/50	0/49	0/24	0/49	0/49	1/48	0/25	0/49	0/49	0/49	1/24	0/49	0/48	0/48	0/24	0/48	0/49	1/49	0/25	0/49	
INGUINAL LYMPH NODES																										
Enlarged	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	
Black	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	1/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	1/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
DIAPHRAGM																											
Nodules	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	1/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/48	1/48	0/24	0/48	0/49	0/49	0/25	0/49	
LIMBS																											
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/25	----	
Infected	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	1/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	2/25	0/49	
PANCREATIC LYMPH NODES																											
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
TEETH																											
Long/overgrown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	1/49	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/48	1/48	0/24	0/48	0/49	0/49	0/25	1/49	
HEPATIC LYMPH NODES																											
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
SCROTAL SACS																											
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
TOTAL HAMSTERS WITH LESIONS	0/99	0/50	0/49	0/49	0/49	0/50	0/50	0/49	0/24	0/49	0/49	0/48	0/25	0/49	0/49	0/49	0/24	0/49	0/48	0/48	0/24	0/48	0/49	0/49	0/25	0/49	
Mass-Location unknown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	

B.2 Second Replicate

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
SKIN/SUBCUTIS																										
Edema, diffuse/focal	14/100	6/50	8/50	6/49	7/49	4/50	5/50	8/50	2/25	8/50	13/50	7/50	3/25	4/50	6/50	4/48	2/23	10/48	6/50	8/49	2/24	4/49	5/50	5/47	3/24	11/50	7/50
Abscess	----	2/50	2/50	1/49	----	----	----	1/50	2/25	1/50	----	----	----	2/50	3/50	1/48	----	1/48	1/50	----	----	----	3/50	----	1/24	----	----
Mass	----	----	1/50	1/49	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	1/50	----	1/24	----	1/50	----	----	----	----
Ulcer	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Exudative	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Necrosis	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Hair loss	----	----	----	----	----	----	----	----	----	1/50	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50
Red, diffuse/focal	2/100	----	----	----	----	----	----	----	1/25	1/50	----	----	----	----	----	----	1/23	----	----	----	----	----	----	----	----	----	----
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Green	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Yellow	----	----	2/50	----	----	----	----	1/50	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----
Thickened	1/100	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Crusty/scaly/dry/flaky	2/100	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lesion	----	----	----	----	1/49	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	18/100	9/50	10/50	8/49	8/49	4/50	5/50	10/50	5/25	10/50	13/50	8/50	3/25	6/50	9/50	5/48	3/23	10/48	8/50	8/49	3/24	4/49	9/50	5/47	5/24	11/50	8/50
MANDIBULAR SALIVARY GLAND																										
Enlarged	----	----	----	----	----	----	----	1/50	1/25	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
Tan	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
Abscess	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Nodule	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Cyst(s)	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Necrosis	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	1/50	1/49	0/49	0/50	0/50	1/50	1/25	0/50	0/50	0/50	0/25	0/50	0/50	2/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
MANDIBULAR LYMPH NODES																										
Enlarged	6/100	1/50	1/50	1/49	2/49	1/50	----	3/50	2/25	1/50	5/50	3/50	----	3/50	2/50	2/48	1/23	3/48	4/50	2/49	----	3/49	5/50	1/47	----	4/50	1/50
Mottleu red	3/100	1/50	1/50	1/49	1/49	2/50	----	2/50	1/25	1/50	4/50	1/50	----	3/50	2/50	----	1/23	2/48	2/50	----	----	4/49	4/50	1/47	----	3/50	----
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
Tan	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	1/49	----	----	----	----	----	----	----
Firm	1/100	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----
Soft	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----
Abscess	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Necrosis	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	6/100	1/50	2/50	1/49	2/49	2/50	0/50	3/50	2/25	1/50	5/50	3/50	0/25	3/50	7/50	2/48	1/23	3/48	4/50	2/49	0/24	4/49	5/50	1/47	0/24	4/50	1/50
MAMMARY GLAND																										
Discolored	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
STERNUM																										
Mottled black	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Inverted	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----
Lesion	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	2/50	0/49	0/49	0/50	0/50	1/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	1/50	0/50
COSTOCHONDRAL																										
Nodule	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
THYMUS																										
Mottled black	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	1/50	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----
TOTAL HAMSTERS WITH LESIONS	0/100	1/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	1/49	0/24	0/49	0/50	1/47	0/24	1/50	0/50
THYROIDS																										
Mottled black	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	1/47	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	1/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	1/50	1/47	0/24	0/50	0/50
PARATHYROIDS																										
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
HEART																										
Mottled black	----	3/50	3/50	5/49	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled red	----	----	----	1/49	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----
Tan/yellow	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
Enlarged	1/100	----	----	----	----	----	----	----	1/25	----	----	----	----	----	1/50	2/48	----	----	----	----	----	----	----	----	1/24	----	----
Small	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----
Firm	----	----	1/50	2/49	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	1/24	----	----
Cyst(s)	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass/growth	----	----	1/50	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Nodule(s)	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Thrombosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesion	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	2/100	3/50	3/50	7/49	0/49	0/50	1/50	0/50	1/25	0/50	2/50	0/50	1/25	0/50	1/50	2/48	0/23	1/48	0/50	0/49	1/24	1/49	0/50	0/47	1/24	0/50	0/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
HEART (AURICLES)																										
Enlarged	25/100	14/50	10/50	9/49	13/49	11/50	18/50	13/50	7/25	7/50	14/50	8/50	4/25	16/50	17/50	11/48	6/23	10/48	13/50	12/49	6/24	11/49	12/50	17/47	6/24	13/50	12/50
Firm	11/100	4/50	3/50	3/49	6/49	4/50	5/50	3/50	1/25	4/50	4/50	3/50	2/25	7/50	9/50	3/48	3/23	3/48	4/50	5/49	4/24	3/49	3/50	6/47	1/24	4/50	3/50
Tan	4/100	1/50	----	----	5/49	2/50	2/50	1/50	2/25	2/50	3/50	2/50	1/25	3/50	3/50	2/48	1/23	2/48	2/50	5/49	5/24	2/49	3/50	6/47	1/24	3/50	2/50
Mottled red	----	----	----	1/49	----	----	----	----	----	----	----	1/50	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----
Mottled white	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled black	----	----	1/50	1/49	----	----	----	1/50	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	26/100	14/50	10/50	9/49	13/49	11/50	18/50	13/50	7/25	8/50	15/50	9/50	4/25	16/50	17/50	11/48	6/23	10/48	13/50	13/49	7/24	12/49	12/50	19/47	6/24	13/50	12/50
ESOPHAGUS																										
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Contained black material	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	1/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
TRACHEA																										
Contained black material	----	30/50	21/50	11/49	----	21/50	24/50	17/50	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Mottled red	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Contained red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/50
TOTAL HAMSTERS WITH LESIONS	0/100	30/50	21/50	11/49	0/49	22/50	24/50	17/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	1/49	0/50	0/47	0/24	0/50	2/50
LUNGS																										
Mottled brown	4/100	1/50	3/49	1/49	3/49	1/50	1/50	----	4/25	1/50	1/50	3/50	2/25	12/50	11/50	7/48	2/23	6/48	4/50	2/49	1/24	5/49	6/50	3/47	2/24	5/50	3/50
Mottled black	2/100	44/50	41/50	32/49	3/49	45/50	46/50	40/50	13/25	17/50	10/50	13/50	5/25	15/50	14/50	9/48	3/23	17/48	8/50	6/49	7/24	12/49	4/50	----	9/24	6/50	3/50
Mottled red	60/100	15/50	17/50	24/49	34/49	18/50	21/50	29/50	14/25	39/50	35/50	33/50	14/25	23/50	28/50	34/48	16/23	32/48	34/50	35/49	14/24	33/49	32/50	36/47	14/24	31/50	38/50
Mottled grey	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	1/24	----	----
Dark spots	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----
Mottled/spotted	1/100	----	----	2/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	1/50	----	----	----	1/50
Nodule	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	3/50	----
Mass	----	----	2/50	1/49	----	----	----	----	----	----	1/50	----	----	1/50	----	1/48	1/23	----	----	----	----	----	----	1/47	----	3/50	----
Cyst(s)	----	----	1/50	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Contained red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	3/50	----
Enlarged, focal/diffuse	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----
Tan, focal/multifocal	----	----	----	----	2/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/50	----
White foci	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	64/100	49/50	49/50	49/49	37/49	50/50	49/50	50/50	24/25	45/50	40/50	39/50	20/25	45/50	47/50	43/48	18/23	42/48	40/50	40/49	20/24	44/49	38/50	38/47	20/24	44/50	40/50
LARYNX																										
Mottled black/contained black material	----	1/50	----	1/49	----	----	2/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	1/50	0/50	1/49	0/49	0/50	2/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe$_2$O$_3$ 5 mg	DP:Fe$_2$O$_3$ 2.5 mg	DP:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	DE:Fe$_2$O$_3$ 5 mg	DE:Fe$_2$O$_3$ 2.5 mg	DE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	COE:Fe$_2$O$_3$ 5 mg	COE:Fe$_2$O$_3$ 2.5 mg	COE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	CSC:Fe$_2$O$_3$ 5 mg	CSC:Fe$_2$O$_3$ 2.5 mg	CSC:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	RTE:Fe$_2$O$_3$ 5 mg	RTE:Fe$_2$O$_3$ 2.5 mg	RTE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	BP:Fe$_2$O$_3$ 2 mg	Gelatin Saline 0.5%
RESPIRATORY LYMPH NODES																										
Mottled black/contained black material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Enlarged	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled red	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	1/50	0/49	0/49	1/50	0/50	0/50	0/25	0/50	0/50	1/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
LIVER																										
Cyst(s)	36/100	13/50	11/50	13/48	13/49	10/50	9/50	11/50	11/25	13/50	16/50	15/50	6/25	10/50	12/50	7/48	7/23	9/48	10/50	10/49	5/24	12/49	11/50	9/47	8/24	15/50	17/50
Tan, diffuse/focal/multifocal	7/100	1/50	2/50	4/48	1/49	----	1/50	2/50	1/25	3/50	2/50	4/50	2/25	2/50	1/50	3/48	1/23	2/48	----	2/49	----	1/49	1/50	2/47	3/24	2/50	1/50
Pitted, granular	2/100	6/50	3/50	3/48	1/49	2/50	3/50	3/50	1/25	5/50	1/50	7/50	1/25	3/50	3/50	1/48	1/23	5/48	2/50	1/49	3/24	1/49	2/50	1/47	3/24	2/50	1/50
Enlarged, thickened	5/100	3/50	2/50	4/48	1/49	1/50	3/50	4/50	2/25	1/50	4/50	2/50	----	5/50	5/50	2/48	----	2/48	----	5/49	1/24	2/49	3/50	2/47	----	5/50	1/50
Soft	2/100	----	4/50	1/48	1/49	----	1/50	1/50	----	1/50	1/50	1/50	1/25	----	1/50	1/48	----	----	----	----	2/24	----	1/50	----	----	----	----
Firm	2/100	----	----	----	----	----	----	1/50	1/25	----	----	----	----	----	----	1/48	----	----	----	1/49	----	----	----	----	----	----	----
Mottled red	8/100	7/50	4/50	4/48	4/49	3/50	3/50	3/50	2/25	----	6/50	4/50	1/25	4/50	7/50	4/48	1/23	7/48	2/50	8/49	1/24	3/49	3/50	5/47	2/24	4/50	----
Mottled brown	3/100	1/50	----	2/48	2/49	1/50	----	1/50	----	1/50	1/50	3/50	----	1/50	1/50	----	----	2/48	1/50	1/49	1/24	1/49	1/50	----	----	2/50	----
Dark brown, diffuse/multifocal	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled black	3/100	1/50	----	2/48	3/49	----	5/50	2/50	2/25	2/50	3/50	1/50	1/25	2/50	2/50	1/48	1/23	1/48	3/50	2/49	----	3/49	2/50	2/47	----	3/50	2/50
Spotted/multiple foci/discolored	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Nodule	----	1/50	----	----	1/49	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	1/24	1/49	----	----	----	----	----
Mass	----	----	----	----	2/49	----	----	----	----	1/50	1/50	2/50	----	1/50	2/50	1/48	----	1/48	----	----	----	----	----	----	----	----	1/50
Abscess	1/100	----	1/50	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesions	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Green foci	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----
TOTAL HAMSTERS WITH LESIONS	50/100	19/50	20/50	23/48	21/49	11/50	20/50	19/50	13/25	18/50	23/50	27/50	8/25	18/50	22/50	14/48	10/23	19/48	16/50	20/49	8/24	19/49	18/50	15/47	11/24	22/50	17/50
GALL BLADDER																										
Distended/enlarged/thickened	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----
Contained fluid (black/yellow/red)	1/100	----	----	----	----	----	----	----	----	----	1/50	----	----	----	1/50	1/48	----	----	1/50	1/49	1/24	----	----	1/47	----	1/50	----
Small	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----
Black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Aplastic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	1/100	0/50	0/50	0/48	0/49	0/50	0/50	0/50	0/25	0/50	2/50	0/50	1/25	0/50	1/50	1/48	0/23	0/48	2/50	1/49	1/24	0/49	0/50	1/47	1/24	1/50	0/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
ADRENAL GLANDS																											
Tan/yellow	28/100	21/50	21/50	13/49	9/49	15/50	24/50	21/50	7/25	10/50	17/50	19/50	5/25	15/50	19/50	15/48	8/23	11/47	12/50	18/49	7/24	14/49	18/49	15/47	8/24	17/50	13/50
Pitted	1/100	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	3/24	----	----	2/47	----	----	----
Enlarged	14/100	10/50	8/50	3/49	7/49	4/50	11/50	11/50	5/25	6/50	11/50	8/50	1/25	7/50	13/50	7/48	4/23	6/47	5/50	10/49	3/24	7/49	11/49	6/47	3/24	8/50	3/50
Red/diffuse, multifocal	1/100	----	----	----	----	----	----	----	----	----	1/50	----	----	1/50	----	----	----	1/47	----	----	----	1/49	1/49	----	----	1/50	----
Black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Grey/white	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Small	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	1/50	----	----	----	1/50	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	1/49	----	----	----	----	----
Mass	----	1/50	----	----	2/49	----	1/50	----	1/25	1/50	2/50	2/50	----	----	1/50	1/48	1/23	----	----	----	----	----	1/49	----	----	----	1/50
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Aplastic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lobular	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
Necrotic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----
Abscess	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	29/100	22/50	22/50	13/49	16/49	16/50	26/50	21/50	8/25	13/50	20/50	22/50	5/25	16/50	22/50	18/48	10/23	12/47	13/50	18/49	8/24	15/49	20/49	17/47	9/24	18/50	16/50
SPLEEN																											
Enlarged	10/100	4/50	6/50	3/49	6/49	1/50	4/50	3/50	4/25	4/49	7/49	9/50	5/25	3/49	7/50	3/48	3/23	5/47	3/50	8/49	4/24	4/49	7/49	6/47	1/24	3/50	4/50
Small	4/100	----	----	2/49	1/49	----	----	2/50	2/25	1/49	1/49	1/50	----	2/49	3/50	----	----	1/47	----	1/49	----	----	1/49	1/47	1/24	3/50	----
Red, diffuse/focal	1/100	1/50	----	----	1/49	----	1/50	----	----	----	----	2/50	----	2/49	----	----	----	----	----	1/49	----	----	----	----	1/24	1/50	----
Nodule	1/100	----	1/50	----	----	1/50	----	1/50	----	1/49	2/49	----	----	2/49	3/50	----	----	----	1/50	----	1/24	----	----	1/47	2/24	6/50	2/50
Mass	5/100	----	----	----	----	----	----	----	----	----	----	1/50	----	----	3/50	1/48	1/23	----	----	----	----	1/49	----	1/47	1/24	5/50	1/50
Pitted/granular	----	----	----	----	----	----	----	----	----	1/49	1/49	----	----	1/49	----	----	----	----	----	----	1/24	----	----	----	----	1/50	----
Ruptured/divided	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Accessory	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	1/24	1/50	----
Mottled black	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan, focal/multifocal	----	----	----	1/49	----	1/50	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----
Grey/white foci	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Cystic/transparent foci	----	1/50	----	----	----	----	1/50	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Blood clots	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	19/100	4/50	7/50	6/49	8/49	3/50	5/50	6/50	6/25	7/49	10/49	13/50	6/25	9/49	14/50	4/48	4/23	7/47	4/50	9/49	4/24	5/49	8/49	9/47	4/24	17/50	7/50
KIDNEYS																											
Tan/pale/grey	25/100	13/50	13/50	9/49	9/49	10/50	8/50	13/50	4/25	5/50	15/50	13/50	7/25	10/50	14/50	16/48	8/23	14/47	9/50	16/49	6/24	13/49	13/49	14/47	9/24	13/50	14/50
Pitted/granular	41/100	18/50	10/50	12/49	14/49	12/50	21/50	18/50	6/25	10/50	20/50	12/50	9/25	16/50	21/50	15/48	8/23	21/47	13/50	18/49	10/24	19/49	20/49	17/47	8/24	18/50	19/50
Enlarged	1/100	1/50	3/50	----	1/49	1/50	----	----	----	----	2/50	----	----	----	----	----	----	----	----	----	----	1/49	----	1/47	----	2/50	1/50
Small	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	1/49	----	----	----	----
Red, diffuse/focal	----	1/50	----	1/49	----	----	1/50	1/50	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	1/50
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
Mottled brown/dark brown	1/100	----	----	1/49	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----
Mass	----	1/50	----	----	2/49	----	1/50	----	1/25	----	1/50	2/50	----	----	1/50	1/48	1/23	----	----	----	----	----	1/49	----	----	----	----
Nodule(s)	----	----	----	1/49	----	----	----	1/50	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
KIDNEYS (contd)																											
Lobular	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Soft	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----
Cyst(s)	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesion	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Covered with red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	46/100	24/50	16/50	17/49	16/49	16/50	23/50	23/50	7/25	13/50	24/50	19/50	12/25	18/50	25/50	20/48	10/23	24/47	16/50	22/49	11/24	20/49	22/49	19/47	11/24	31/50	25/50
URINARY BLADDER																											
Contained calculi	----	----	----	1/49	----	1/50	1/50	----	----	1/49	----	1/50	----	----	----	3/48	----	----	1/50	1/49	----	1/49	1/49	2/47	----	3/50	----
Distended	2/100	1/49	----	----	1/49	1/50	1/50	----	----	----	----	----	1/25	----	----	----	----	1/47	----	----	3/24	----	2/49	1/47	----	1/50	----
Thickened walls	----	----	----	----	1/49	----	----	1/50	----	2/49	----	----	----	----	1/50	----	----	1/47	2/50	----	1/24	1/49	1/49	----	----	1/50	1/50
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50
Small	----	1/49	----	----	----	1/50	----	----	----	----	----	----	----	1/50	----	----	----	----	----	1/49	----	----	----	----	----	1/50	----
Contained fluid, red/dark brown	1/100	----	----	1/49	----	----	1/50	----	1/25	----	----	----	----	----	1/50	----	----	1/47	----	1/49	----	----	1/49	1/47	----	2/50	----
TOTAL HAMSTERS WITH LESIONS	3/100	2/49	0/50	2/49	2/49	2/50	2/50	1/50	1/25	3/49	0/50	1/50	1/25	1/50	2/50	3/48	0/23	2/47	3/50	3/49	4/24	3/49	4/49	3/47	0/24	6/50	2/50
TESTES																											
Small/degenerated	31/100	19/49	18/50	17/49	17/49	17/50	15/50	18/50	10/25	14/49	16/50	15/50	9/25	17/50	18/50	15/48	7/23	16/47	15/50	12/49	6/24	19/49	13/49	14/47	8/24	22/50	11/50
Aplastic	----	----	----	----	----	----	----	----	1/25	1/49	----	1/50	----	1/50	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Dark red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50
Grey	----	----	----	1/49	----	1/50	----	----	1/25	1/49	----	----	1/25	----	----	----	1/23	----	----	----	----	1/49	----	----	----	----	----
Dark brown	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/23	----	----	----	----	----	----	----	----	----	----
Covered with red material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Abscess/infected	1/100	----	----	----	----	----	----	----	----	1/49	----	----	1/25	----	----	----	1/23	----	----	----	----	----	----	----	----	----	----
Enlarged	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	31/100	19/49	18/50	18/49	17/49	18/50	15/50	18/50	12/25	14/49	16/50	16/50	10/25	17/50	18/50	15/48	8/23	16/47	15/50	12/49	6/24	21/49	13/49	14/47	8/24	22/50	12/50
EPIDIDYMIS																											
Small/degenerated	19/100	12/49	9/50	7/49	7/49	9/50	8/50	10/50	3/25	7/49	5/50	7/50	3/25	8/50	11/50	10/48	1/23	7/47	7/50	7/49	5/24	6/49	8/49	9/47	----	15/50	6/50
Flaccid	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Aplastic	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Abscess/infected	1/100	----	----	----	1/49	2/50	----	----	1/25	1/49	1/50	----	----	----	----	----	----	1/47	----	1/49	----	1/49	1/49	----	----	1/50	1/50
Enlarged	----	----	----	----	----	----	----	----	1/25	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Black	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesion	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----
Cystic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----
Mass	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	20/100	12/49	9/50	7/49	8/49	11/50	8/50	10/50	4/25	8/49	6/50	7/50	3/25	10/50	11/50	10/48	1/23	8/47	7/50	8/49	5/24	8/49	8/49	9/47	0/24	16/50	7/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
SEMINAL VESICLES																										
Small	18/100	10/49	7/50	6/49	2/49	10/50	8/50	10/50	4/25	6/49	6/50	6/50	3/25	7/50	10/50	8/48	1/23	7/47	6/50	5/49	4/24	7/49	7/49	6/47	----	15/50	6/50
Flaccid	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----
Red	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
Yellow	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	2/50	----
Contained fluid, red/yellow/ brown	1/100	----	----	----	----	----	1/50	----	----	----	1/50	----	----	----	----	----	----	----	1/50	1/49	----	1/49	1/49	----	1/24	----	----
Abscess/infected	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50
Aplastic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	2/49	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	19/100	10/49	7/50	6/49	2/49	10/50	9/50	10/50	4/25	8/49	7/50	6/50	4/25	7/50	10/50	8/48	1/23	7/47	6/50	6/49	4/24	9/49	8/49	6/47	1/24	17/50	7/50
PROSTATE																										
Small	4/100	1/49	----	----	----	----	----	----	----	----	2/50	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	1/50	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Cystic	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	4/100	1/49	0/50	0/49	1/49	0/50	0/50	0/50	0/25	0/49	2/50	0/50	0/25	0/50	0/50	1/48	0/23	0/47	0/50	0/49	0/24	1/49	0/49	0/47	0/24	1/50	0/50
PANCREAS																										
Adhesions	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	1/47	----	----	----
Mottled black	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan/yellow	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----
Fatty infiltration	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Abscess	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Nodules	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	1/100	0/50	1/50	0/48	0/49	0/50	0/50	0/50	0/25	0/49	0/50	1/50	1/25	0/49	0/50	0/48	0/23	0/47	1/50	0/49	0/24	1/49	0/49	1/47	0/24	0/50	0/50
STOMACH																										
Black foci, mucosa/serosa	5/100	5/50	2/50	2/49	5/49	2/50	----	1/50	1/25	1/49	2/50	2/50	2/25	1/50	1/50	2/48	----	3/47	1/50	5/49	1/24	4/49	1/49	6/47	5/24	5/50	2/50
Contained material, red/ brown-green	----	1/50	1/50	----	1/49	1/50	2/50	----	----	----	3/50	1/50	2/25	----	----	1/48	----	2/47	----	----	2/24	1/49	1/49	1/47	----	----	3/50
Distended/gas filled	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan/yellow	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled red, mucosa/serosa	----	2/50	----	----	----	----	----	----	2/25	----	----	1/50	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----
Mottled brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Thickened	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Edematous	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Nodules	1/100	1/50	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
STOMACH (contd)																											
Dark foci, mucosa/serosa, diffuse/focal	2/100	----	----	----	1/49	----	----	1/50	1/25	----	----	----	----	----	----	----	----	----	1/50	----	----	----	1/49	----	----	----	----
Cyst(s)	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	8/100	8/50	5/50	3/49	8/49	3/50	2/50	2/50	3/25	1/49	5/50	4/50	5/25	1/50	1/50	3/48	0/23	6/47	2/50	5/49	2/24	5/49	3/49	7/47	5/24	5/50	5/50
DUODENUM																											
Contained material/fluid (red/brown-green)	1/100	----	----	----	----	----	----	----	----	----	----	1/50	3/25	----	2/50	----	1/23	----	1/50	2/49	1/24	----	----	----	----	1/50	1/50
Tan/yellow/white	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	1/24	----	----
Nodule	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	1/100	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Herniated	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	----	----	----	1/49	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesion	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Distended/gas filled/enlarged	----	----	1/50	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	2/100	0/49	1/50	0/48	3/49	0/50	0/50	0/50	0/25	1/49	1/50	2/50	3/25	0/50	3/50	0/48	1/23	0/47	1/50	2/49	1/24	0/49	0/49	0/47	1/24	1/50	1/50
JEJUNUM																											
Contained material/fluid (red/brown-green)	1/100	----	----	----	----	----	1/50	1/50	----	----	----	----	2/25	----	2/50	----	----	1/47	1/50	4/49	1/24	----	----	----	----	1/50	1/50
Distended/gas filled	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan/yellow/white	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	1/24	----	----
Mass	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Herniated	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	1/100	----	----	----	2/49	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	1/49	----	----	----	1/47	1/24	----	----
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	1/50
Intussusception	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----
Nodules	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	2/100	0/49	0/50	0/48	4/49	0/50	1/50	2/50	0/25	0/49	1/50	0/50	2/25	0/50	3/50	0/48	0/23	1/47	1/50	5/49	1/24	0/49	0/49	2/47	2/24	1/50	2/50
ILEUM																											
Contained material/fluid (red/brown-green)	1/100	----	----	----	----	----	----	1/50	----	----	----	----	[illegible]	----	2/50	1/48	----	1/47	1/50	4/49	1/24	----	----	----	----	1/50	1/50
Distended/gas filled	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----
Tan/yellow/white	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	1/24	----	----
Green	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Herniated	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Intussusception	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----
Red	1/100	----	----	----	2/49	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	1/49	----	----	----	1/47	1/24	----	----
TOTAL HAMSTERS WITH LESIONS	2/100	0/49	0/50	0/48	4/49	0/50	0/50	2/50	0/25	0/49	1/50	0/50	3/25	1/50	3/50	1/48	0/23	1/47	1/50	5/49	2/24	0/49	0/49	1/47	2/24	1/50	1/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
CECUM																											
Contained material/fluid (red/brown-green)	1/100	2/49	----	----	----	----	1/50	2/50	----	----	----	1/50	2/25	----	2/50	1/48	1/23	----	1/50	4/49	----	----	3/49	2/47	----	1/50	2/50
Distended/gas filled/enlarged	1/100	----	1/50	----	1/49	----	2/50	----	----	1/49	----	----	----	2/50	----	----	----	----	2/50	1/49	1/24	----	2/49	2/47	----	----	----
Nodule	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/23	----	----	----	----	----	----	1/47	----	----	1/50
Mass	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	1/49	----	----	----	----	----
Abscess	2/100	----	----	----	1/49	----	1/50	----	2/25	1/49	----	----	----	----	----	----	----	2/47	----	----	----	----	----	----	----	1/50	1/50
Tan/yellow	----	----	----	----	----	1/50	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	1/50	----
Herniated	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red, diffuse/multifocal	1/100	----	----	----	1/49	----	1/50	----	----	----	----	----	----	----	----	----	----	----	1/50	1/49	----	----	1/49	----	----	----	----
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----
Grey	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Thickened	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	5/100	2/49	1/50	0/48	5/49	1/50	6/50	2/50	2/25	2/49	0/50	1/50	2/25	2/50	3/50	1/48	1/23	2/47	4/50	5/49	1/24	1/49	6/49	5/47	1/24	3/50	4/50
COLON																											
Contained material/fluid (red/brown-green)	----	1/49	----	----	----	----	----	1/50	----	----	----	----	2/25	----	1/50	----	----	----	1/50	3/49	----	----	----	----	----	2/50	1/50
Distended/gas filled	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Abscess	1/100	----	----	----	----	----	----	----	1/25	----	----	----	----	----	1/50	----	----	1/47	----	----	----	----	----	----	----	----	1/50
Tan/yellow/white	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	1/50	----
Obstruction	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	1/49	----	----	----	----
Mass	1/100	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Nodule	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----	----	----	----
Green, diffuse/focal	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Intussusception	1/100	1/49	1/50	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	1/49	1/24	1/49	----	----	----	----	----
Empty	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Herniated	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Protruding	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	2/100	2/49	1/50	1/48	2/49	0/50	1/50	1/50	1/25	0/49	0/50	0/50	2/25	0/50	2/50	0/48	0/23	3/47	1/50	4/49	1/24	2/49	1/49	1/47	1/24	3/50	2/50
RECTUM																											
Contained material/fluid (red/brown-green)	----	----	----	----	----	----	----	----	----	----	----	----	2/25	----	1/50	----	----	----	1/50	2/49	----	----	----	----	----	1/50	1/50
Herniated	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Prolapse	----	1/49	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50
Tan/yellow/white	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/24	----	----
Distended/gas filled	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	1/49	0/50	0/48	2/49	0/50	0/50	1/50	0/25	0/49	0/50	0/50	2/25	0/50	1/50	0/48	0/23	0/47	1/50	2/49	1/24	0/49	0/49	0/47	1/24	1/50	2/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
MESENTERIC LYMPH NODES																											
Tan/pale/yellow	2/100	----	----	----	----	----	1/50	1/50	----	2/49	3/50	2/50	1/25	3/50	----	1/48	1/23	2/47	----	4/49	----	1/49	1/49	2/47	----	3/50	2/50
Enlarged	18/100	6/49	10/50	9/48	5/49	7/50	10/50	12/50	4/25	9/49	14/50	12/50	3/25	8/50	13/50	9/48	5/23	10/47	12/50	9/49	5/24	6/49	8/49	10/47	3/24	12/50	4/50
Mottled/dark red	----	----	----	----	----	----	1/50	----	----	1/49	1/50	----	----	----	----	----	----	1/47	----	2/49	----	----	----	----	----	----	----
Abscess	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50
Mottled black/contained black material	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	1/50	----	----	1/49	----	1/47	----	----	----
Dark color	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	1/50	----	----	----	1/50	----	----	----	----	1/48	----	----	----	----	----	1/49	----	----	----	----	1/50
Brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	1/47	----	----	----
Soft	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	1/47	----	----	----
Cyst(s)	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesions	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	18/100	6/49	10/50	9/48	6/49	7/50	12/50	12/50	4/25	9/49	14/50	12/50	3/25	8/50	13/50	11/48	5/23	10/47	12/50	9/49	5/24	7/49	8/49	10/47	3/24	12/50	6/50
SKELETAL MUSCLE																											
Brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	1/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
SCIATIC NERVE	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
EYES																											
White/grey/corneal opacity, focal/diffuse	2/100	1/50	3/50	2/49	2/49	----	1/50	2/50	3/25	1/50	----	----	1/25	----	2/50	2/48	1/23	1/48	2/50	3/49	2/24	3/49	1/50	1/47	1/24	3/50	2/50
Small	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Crust formation	2/100	----	----	----	1/49	----	----	1/50	----	1/50	----	----	1/25	----	----	----	----	1/48	----	1/49	----	1/49	----	2/47	----	----	----
Exudative	----	----	2/50	----	----	----	1/50	1/50	----	----	----	----	1/25	----	----	----	----	----	----	1/49	----	----	----	1/47	----	----	----
Degenerated/missing	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----
Red	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----
Discolored	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Protruding	----	----	----	----	----	----	----	----	----	----	1/50	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----
Hard	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----
Orbital abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	4/100	1/50	5/50	2/49	3/49	0/50	3/50	3/50	3/25	2/50	1/50	0/50	2/25	1/50	2/50	2/48	1/23	3/48	2/50	4/49	2/24	4/49	1/50	4/47	1/24	3/50	2/50
EAR																											
Abscess	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	1/50	0/49	0/49	0/50	0/50	0/50	0/25	1/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	1/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
NASAL TURBINATES																											
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Contained red material	----	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	1/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe$_2$O$_3$ 5 mg	DP:Fe$_2$O$_3$ 2.5 mg	DP:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	DE:Fe$_2$O$_3$ 5 mg	DE:Fe$_2$O$_3$ 2.5 mg	DE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	COE:Fe$_2$O$_3$ 5 mg	COE:Fe$_2$O$_3$ 2.5 mg	COE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	CSC:Fe$_2$O$_3$ 5 mg	CSC:Fe$_2$O$_3$ 2.5 mg	CSC:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	RTE:Fe$_2$O$_3$ 5 mg	RTE:Fe$_2$O$_3$ 2.5 mg	RTE:Fe$_2$O$_3$ 1.25 mg	Solvent + Fe$_2$O$_3$, 5 mg	BP:Fe$_2$O$_3$ 2 mg	Gelatin Saline 0.5%
BRAIN																											
Mottled red	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled brown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Covered with red material	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Blood clot	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----
Edematous	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	2/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	1/50	0/50	0/25	1/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
PITUITARY GLAND																											
Dark red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	1/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
SPINAL CORD/COLUMN																											
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
CHEEK POUCH																											
Mass	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	1/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	1/25	0/50	0/50	0/48	0/23	1/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
THORACIC CAVITY																											
Contained fluid	3/100	1/50	----	----	4/49	2/50	3/50	----	1/25	2/50	3/50	4/50	----	1/50	2/50	1/48	----	1/48	1/50	4/49	1/24	3/49	2/50	1/47	1/24	5/50	1/50
Contained red material/blood filled	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----
TOTAL HAMSTERS WITH LESIONS	3/100	1/50	0/50	1/49	4/49	2/50	3/50	0/50	1/25	2/50	3/50	4/50	0/25	1/50	2/50	1/48	0/23	1/48	1/50	4/49	1/24	3/49	2/50	2/47	1/24	5/50	1/50
ABDOMINAL CAVITY																											
Contained fluid	4/100	2/50	5/50	4/49	3/49	3/50	----	1/50	1/25	3/50	2/50	4/50	2/25	3/50	1/50	----	1/23	2/48	3/50	1/49	2/24	2/49	1/50	1/47	1/24	5/50	1/50
Contained red material/blood filled/blood clot	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	1/50	1/48	----	----	----	----	----	----	----	1/47	1/24	----	----
Mass	----	----	----	----	----	----	----	1/50	----	----	1/50	----	----	----	----	1/48	----	----	----	----	----	1/49	----	----	----	----	----
Abscess/contained green material	----	----	----	----	1/49	----	----	----	1/25	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Cyst(s)	----	----	----	----	----	----	----	1/50	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	4/100	2/50	5/50	4/49	4/49	3/50	0/50	3/50	2/25	3/50	4/50	4/50	2/25	3/50	2/50	1/48	1/23	2/48	3/50	1/49	2/24	3/49	1/50	2/47	2/24	5/50	1/50
PAW(S)																											
Swollen	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3, 5 mg	DP:Fe_2O_3, 2.5 mg	DP:Fe_2O_3, 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3, 5 mg	DE:Fe_2O_3, 2.5 mg	DE:Fe_2O_3, 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3, 5 mg	COE:Fe_2O_3, 2.5 mg	COE:Fe_2O_3, 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3, 5 mg	CSC:Fe_2O_3, 2.5 mg	CSC:Fe_2O_3, 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3, 5 mg	RTE:Fe_2O_3, 2.5 mg	RTE:Fe_2O_3, 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3, 2 mg	Gelatin Saline 0.5%
PAW(S) (contd)																											
Grey	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	1/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
MOUTH																											
Contained red material/ hemorrhage	----	2/50	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	2/50	0/50	0/49	1/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
PELVIC/LUMBAR LYMPH NODES																											
Enlarged	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	1/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
RENAL LYMPH NODES																											
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	1/49	----	----	----	----	----
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	1/49	0/24	1/49	0/50	0/47	0/24	0/50	0/50
MANDIBLE																											
Abscess	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/48	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	1/24	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	1/50	0/50	0/50	0/25	0/50	0/50	1/48	0/23	0/48	0/50	0/49	1/24	0/49	0/50	0/47	0/24	0/50	0/50
SKULL																											
Contained red material	----	1/50	----	----	----	----	----	1/50	----	----	1/50	----	----	----	----	----	----	----	1/50	----	1/24	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	1/50	0/50	0/49	0/49	0/50	0/50	1/50	0/25	0/50	1/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	1/50	0/49	1/24	0/49	0/50	0/47	0/24	0/50	0/50
AUXILIARY LYMPH NODES																											
Enlarged	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	----	----	1/49	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Tan	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	1/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
INGUINAL LYMPH NODES																											
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----
Black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	1/47	0/24	0/50	0/50
DIAPHRAGM																											
Nodules	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/27	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50

SUMMARY OF GROUP INCIDENCES OF GROSS OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
LIMBS																											
Mass	1/100	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Infected	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	1/100	0/50	0/50	0/49	0/49	1/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
PANCREATIC LYMPH NODES																											
Red	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Enlarged	----	----	----	----	----	----	----	----	----	----	----	1/50	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	1/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
TEETH																											
Long/overgrown	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
HEPATIC LYMPH NODES																											
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----
Red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/49	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	0/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	1/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50
SCROTAL SACS																											
Abscess	1/100	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TOTAL HAMSTERS WITH LESIONS	1/100	0/50	0/50	0/49	0/49	0/50	0/50	0/50	0/25	0/50	0/50	0/50	0/25	0/50	0/50	0/48	0/23	0/48	0/50	0/49	0/24	0/49	0/50	0/47	0/24	0/50	0/50

APPENDIX C

SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

C.1 First Replicate - High Dose

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138

ORGAN Lesion	DPOO 5.00	DPFO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCON	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
LUNGS														
PARTICLES	46/46	45/45	43/43	41/41	47/47	44/44	41/41	0/95	3/42	21/21	25/25	22/22	20/20	22/22
INFLAM REACTION	45/46	44/45	26/43	33/41	11/47	9/44	19/41	2/95	6/42	12/21	13/25	10/22	2/20	9/22
GRANULOMA	41/46	43/45	32/43	34/41	1/47	3/44	9/41	1/95	0/42	3/21	1/25	4/22	1/20	1/22
FIBROSIS	21/46	22/45	4/43	17/41	3/47	1/44	4/41	3/95	3/42	3/21	1/25	2/22	2/20	2/22
HYPERPLASIA ADENO	37/46	43/45	22/43	30/41	26/47	22/44	24/41	25/95	16/42	15/21	13/25	12/22	10/20	10/22
HYPERPLASIA PAPIL	19/46	12/45	11/43	19/41	3/47	1/44	7/41	2/95	7/42	1/21	0/25	1/22	0/20	1/22
METAPLASIA, CILIARY	25/46	33/45	4/43	13/41	3/47	0/44	8/41	0/95	2/42	2/21	0/25	2/22	0/20	3/22
METAPLASIA, SQUAMOUS	6/46	2/45	5/43	18/41	2/47	2/44	4/41	1/95	3/42	0/21	0/25	1/22	1/20	1/22
PROLIF FIBROBLASTS	9/46	11/45	2/43	14/41	3/47	2/44	5/41	3/95	1/42	2/21	1/25	1/22	2/20	1/22
MONONUCLE CELL INFIL	38/46	31/45	31/43	27/41	26/47	22/44	19/41	32/95	31/42	19/21	19/25	17/22	12/20	14/22
CONGESTION	33/46	34/45	31/43	29/41	38/47	36/44	25/41	71/95	28/42	21/21	23/25	18/22	14/20	15/22
HEMORRHAGE	9/46	8/45	6/43	4/41	5/47	1/44	4/41	11/95	4/42	3/21	1/25	2/22	4/20	0/22
PNEUMONIA	11/46	12/45	21/43	18/41	21/47	17/44	15/41	49/95	15/42	12/21	14/25	10/22	11/20	12/22
EMPHYSEMA	38/46	43/45	32/43	33/41	31/47	22/44	20/41	58/95	27/42	16/21	16/25	18/22	13/20	17/22
PLEURA														
PARTICLES	36/45	40/45	9/43	21/40	4/47	5/44	2/38	0/95	0/42	6/21	4/25	7/22	3/20	2/22
INFLAM REACTION	24/45	20/45	3/43	9/40	4/47	1/41	2/38	4/95	1/42	4/21	4/25	3/22	2/20	3/22
FIBROSIS	33/45	41/45	8/43	20/40	3/47	5/44	7/38	4/95	1/42	2/21	3/25	3/22	0/20	2/22
PROLIFERATION	17/45	24/45	21/43	18/40	6/47	10/44	11/38	9/95	1/42	3/21	3/25	5/22	4/20	4/22

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TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

16138

ORGAN Lesion	DPOO 5.00	DPFO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCON	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
PLEURA														
MONONUCLE CELL INFIL	9/45	5/45	1/43	4/40	0/47	0/44	0/38	4/95	1/42	0/21	1/25	2/22	0/20	1/22
PAPILLARY STRUCTURES	0/45	1/45	0/43	0/40	0/47	0/44	0/38	0/95	0/42	0/21	0/25	0/22	0/20	0/22
LARYNX														
PARTICLES	35/43	37/38	6/33	9/30	11/42	2/33	4/32	0/90	0/41	3/20	3/23	5/21	1/13	7/20
INFLAM REACTION	4/43	2/38	3/33	1/30	5/42	4/33	6/32	0/90	1/41	5/20	1/23	1/21	2/13	1/20
ECTASIA (GLANDS)	8/43	3/38	3/33	4/30	5/42	7/33	3/32	11/90	6/41	4/20	2/23	2/21	2/13	2/20
CYST (GLANDS)	3/43	2/38	2/33	2/30	5/42	6/33	5/32	6/90	4/41	2/20	0/23	2/21	0/13	1/20
MONONUCLE CELL INFIL	1/43	4/38	3/33	4/30	6/42	3/33	2/32	0/90	0/41	2/20	0/23	3/21	0/13	0/20
TRACHEA														
PARTICLES	43/43	45/45	17/34	26/37	21/43	6/35	7/33	0/91	0/40	11/21	11/21	15/21	9/15	11/19
INFLAM REACTION	4/43	1/45	10/34	0/37	2/43	3/35	5/33	0/91	2/40	3/21	3/21	3/21	2/15	1/19
MONONUCLE CELL INFIL	1/43	4/45	4/34	7/37	14/43	3/35	5/33	2/91	3/40	7/21	2/21	5/21	2/15	4/19
ECTASIA (GLANDS)	11/43	12/45	15/34	7/37	10/43	14/35	9/33	21/91	12/40	13/21	7/21	3/21	3/15	8/19
CYSTS (GLANDS)	2/43	5/45	2/34	3/37	2/43	3/35	5/33	8/91	2/40	1/21	2/21	0/21	1/15	3/19
HYPERPLASIA (MUCOSA)	0/43	1/45	0/34	1/37	1/43	0/35	5/33	1/91	0/40	0/21	0/21	0/21	0/15	0/19
THYROIDS														
ECTASIA	26/43	14/43	30/40	19/35	27/43	29/36	17/32	53/90	23/38	6/20	15/24	11/20	11/17	12/17
CYST	17/43	11/43	14/40	12/35	12/43	11/36	15/32	41/90	16/38	9/20	10/24	5/20	9/17	4/17
AMYLOIDOSIS	8/43	12/43	14/40	6/35	9/43	4/36	3/32	17/90	11/38	7/20	5/24	6/20	7/17	4/17

LG138

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

ORGAN Lesion	DPOO 5.00	DPFO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCON	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
THYROIDS														
ATROPHY	7/43	11/43	4/40	5/35	5/43	2/36	3/32	25/90	8/38	7/20	3/24	2/20	1/17	1/17
PARATHYROIDS														
HYPERPLASIA	3/39	5/32	1/35	1/28	2/39	0/30	1/26	3/72	1/35	1/17	3/21	1/17	2/12	0/16
ESOPHAGUS														
BRAIN														
CONGESTION	32/39	34/38	29/31	29/36	34/40	25/36	25/26	45/70	26/35	16/17	17/23	14/17	11/13	12/14
HEMORRHAGE	4/39	2/38	1/31	2/36	2/40	3/36	4/26	5/70	2/35	1/17	1/23	1/17	2/13	1/14
EDEMA	13/39	17/38	8/31	6/36	18/40	15/36	14/26	34/70	19/35	8/17	11/23	7/17	6/13	6/14
SPINAL CORD														
CONGESTION	7/34	4/35	3/28	3/35	11/35	6/36	8/20	5/65	11/35	4/17	6/19	3/14	1/11	2/13
EDEMA	1/34	0/35	1/28	0/35	0/35	0/36	0/20	2/65	3/35	0/17	2/19	2/14	0/11	2/13
EYES														
CATARACT	4/28	2/26	3/25	4/25	2/37	3/26	6/24	8/59	1/23	0/10	0/ 7	0/ 7	1/12	0/10
FIBROSIS	0/28	1/26	0/25	0/25	1/37	0/26	1/24	2/59	0/23	0/10	0/ 7	0/ 7	0/12	1/10
PITUITARY														
VACUOLIZATION	30/34	30/33	29/30	27/28	32/38	28/29	27/29	66/76	29/33	17/17	14/18	10/12	11/12	12/12
CYST	3/34	0/33	5/30	1/28	0/38	0/29	4/29	3/76	1/33	1/17	1/18	0/12	1/12	0/12
CONGESTION	19/34	12/33	19/30	11/28	18/38	18/29	17/29	24/76	9/33	10/17	9/18	9/12	6/12	4/12
AMYLOIDOSIS	1/34	3/33	4/30	2/28	6/38	3/29	0/29	3/76	3/33	3/17	3/18	1/12	1/12	0/12

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138

ORGAN Lesion	DPOO 5.00	DPFO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCON	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
ADRENAL CORTEX														
HYPERPLASIA	20/41	10/41	21/38	16/37	10/43	16/37	16/34	39/83	16/41	8/21	8/23	9/18	7/16	7/16
CONGESTION	12/41	2/41	0/38	1/37	0/43	2/37	0/34	2/83	4/41	2/21	0/23	1/18	0/16	0/16
HEMORRHAGE	17/41	26/41	14/38	23/37	13/43	16/37	10/34	27/83	15/41	11/21	8/23	7/18	5/16	6/16
BROWN PIGMENT	20/41	11/41	10/38	3/37	9/43	5/37	9/34	39/83	13/41	6/21	9/23	3/18	6/16	9/16
AMYLOIDOSIS	[illegible]	31/41	28/38	27/37	20/43	18/37	17/34	41/83	19/41	16/21	12/23	12/18	12/16	7/16
VACUOLIZATION	2/41	0/41	1/38	1/37	4/43	1/37	1/34	8/83	0/41	0/21	2/23	3/18	0/16	1/16
ATROPHY	1/41	1/41	0/38	1/37	0/43	2/37	0/34	0/83	1/41	0/21	1/23	0/18	0/16	0/16
ADRENAL MEDULLA														
CONGESTION	12/41	8/41	5/38	7/37	11/43	9/37	5/34	15/83	7/41	5/21	6/23	7/18	2/16	5/16
BROWN PIGMENT	2/41	2/41	1/38	1/37	2/43	0/37	0/34	4/83	2/41	1/21	1/23	0/18	1/16	2/16
MONONUCLE CELL INFIL	8/41	3/41	4/38	3/37	4/43	4/37	1/34	11/83	6/41	2/21	2/23	4/18	1/16	4/16
ATROPHY	2/41	3/41	0/38	1/37	1/43	1/37	0/34	4/83	1/41	0/21	0/23	0/18	1/16	1/16
SPLEEN														
BROWN PIGMENT	17/38	19/43	14/36	19/33	15/46	20/36	13/33	31/82	16/39	9/20	10/20	9/18	7/16	9/17
FIBROSIS	0/38	1/43	0/36	1/33	2/46	1/36	0/33	2/82	0/39	0/20	0/20	0/18	0/16	0/17
AMYLOIDOSIS	16/38	21/43	18/36	9/33	16/46	12/36	12/33	31/82	14/39	10/20	9/20	7/18	10/16	6/17
HYPOPLASIA	12/38	11/43	12/36	6/33	13/46	7/36	6/33	17/82	11/39	7/20	6/20	1/18	6/16	3/17
HYPERPLASIA	4/38	9/43	6/36	5/33	10/46	7/36	8/33	7/82	5/39	3/20	4/20	2/18	2/16	2/17
CONGESTION	3/38	2/43	0/36	3/33	2/46	3/36	2/33	2/82	2/39	1/20	0/20	0/18	0/16	1/17

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

IG138 ORGAN Lesion	DPOO 5.00	DPFO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCON	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
SPLEEN														
HEMORRHAGE	3/38	6/43	7/36	4/33	4/46	5/36	3/33	3/82	1/39	5/20	2/20	0/18	1/16	1/17
PANCREAS														
FATTY INFILTRATION	2/38	0/37	3/33	2/31	2/45	6/34	4/31	3/73	0/35	1/18	1/20	1/18	3/12	0/15
INFLAMMATION	0/38	0/37	0/33	0/31	4/45	1/34	0/31	2/73	0/35	0/18	0/20	0/18	0/12	0/15
CYST (DUCTS)	4/38	2/37	4/33	3/31	2/45	8/34	8/31	7/73	1/35	6/18	4/20	1/18	1/12	2/15
HYPERPLASIA	0/38	0/37	2/33	0/31	0/45	1/34	2/31	0/73	0/35	0/18	0/20	1/18	0/12	0/15
HEART														
CONGESTION	21/43	20/43	23/41	20/40	22/45	18/40	24/38	36/91	21/42	9/21	15/24	7/20	8/20	11/21
HEMORRHAGE	8/43	4/43	3/41	1/40	3/45	3/40	1/38	4/91	6/42	0/21	3/24	1/20	0/20	0/21
INFLAMMATION	6/43	6/43	5/41	8/40	4/45	3/40	6/38	15/91	5/42	1/21	2/24	0/20	4/20	3/21
FIBROSIS	3/43	6/43	5/41	6/40	1/45	2/40	5/38	12/91	2/42	4/21	4/24	2/20	4/20	3/21
ARTERITIS. (PERI)	5/43	1/43	0/41	6/40	0/45	0/40	0/38	1/91	0/42	0/21	0/24	0/20	0/20	0/21
PARTICLES	1/43	2/43	0/41	0/40	0/45	0/40	0/38	0/91	0/42	0/21	0/24	0/20	0/20	0/21
THROMBOSIS	5/43	9/43	7/41	7/40	4/45	3/40	6/38	19/91	4/42	2/21	3/24	2/20	4/20	4/21
MINERALIZATION	12/43	9/43	7/41	5/40	8/45	6/40	9/38	16/91	7/42	3/21	5/24	6/20	7/20	6/21
KIDNEYS														
NEPHROPATHY	36/42	37/40	36/43	33/36	40/45	36/41	31/35	87/90	34/40	21/21	18/21	21/22	14/18	16/19
NEPHROSCLEROSIS	28/42	28/40	25/43	22/36	22/45	23/41	15/35	58/90	24/40	14/21	11/21	9/22	10/18	11/19
AMYLOIDOSIS	19/42	26/40	17/43	17/36	13/45	9/41	8/35	29/90	16/40	13/21	7/21	8/22	9/18	4/19

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

16138

ORGAN Lesion	DPOO 5.00	DPFO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCON	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
KIDNEYS														
MINERALIZATION	36/42	32/40	36/43	30/36	37/45	38/41	30/35	76/90	30/40	19/21	18/21	14/22	17/18	16/19
CONGESTION	10/42	12/40	11/43	8/36	17/45	11/41	11/35	18/90	9/40	4/21	4/21	9/22	2/18	4/19
MONONUCLE CELL INFIL	4/42	9/40	10/43	9/36	11/45	7/41	7/35	9/90	7/40	1/21	1/21	3/22	5/18	2/19
INFLAMMATION	0/42	1/40	0/43	0/36	2/45	0/41	0/35	0/90	1/40	0/21	0/21	0/22	2/18	0/19
METAPLA (PELVIS)	0/42	0/40	0/43	1/36	1/45	1/41	0/35	0/90	0/40	0/21	0/21	0/22	2/18	0/19
LIVER														
CONGESTION	38/42	39/43	33/40	30/35	35/44	28/34	25/34	72/82	30/38	15/20	22/24	17/19	13/16	12/17
HEMORRHAGE	6/42	3/43	5/40	3/35	6/44	3/34	5/34	11/82	6/38	1/20	2/24	2/19	6/16	1/17
DEGENERATION, VACUOL	12/42	13/43	8/40	7/35	13/44	6/34	9/34	27/82	13/38	4/20	4/24	1/19	5/16	7/17
DEGENERATION, GRANUL	25/42	21/43	8/40	12/35	9/44	11/34	14/34	45/82	24/38	8/20	8/24	6/19	6/16	6/17
NECROSIS	7/42	3/43	0/40	2/35	5/44	0/34	2/34	7/82	4/38	2/20	0/24	2/19	2/16	1/17
AMYLOIDOSIS	23/42	26/43	25/40	19/35	17/44	17/34	8/34	37/82	14/38	11/20	11/24	10/19	12/16	6/17
BROWN PIGMENT	33/42	31/43	23/40	21/35	19/44	17/34	21/34	42/82	19/38	12/20	14/24	11/19	9/16	14/17
INFLAMMATORY CELL	35/42	37/43	36/40	29/35	34/44	24/34	25/34	68/82	25/38	13/20	19/24	17/19	13/16	11/17
EXTRAMEDUL HEMATOPOL	12/42	11/43	13/40	11/35	14/44	11/34	13/34	29/82	11/38	3/20	6/24	4/19	4/16	5/17
PARTICLES	5/42	6/43	2/40	3/35	1/44	1/34	5/34	0/82	0/38	0/20	0/24	1/19	0/16	1/17
PROLIFERATION	28/42	30/43	24/40	16/35	17/44	17/34	8/34	39/82	17/38	13/20	13/24	13/19	13/16	6/17
CYST	10/42	13/43	13/40	6/35	10/44	10/34	7/34	22/82	8/38	6/20	7/24	3/19	9/16	4/17

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

16138

ORGAN Lesion	DPOO 5.00	DPFO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCON	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
GALL BLADDER														
INFLAMMATION	0/24	0/20	1/18	1/19	0/25	0/23	0/18	1/42	0/18	0/11	1/11	1/ 7	0/12	0/ 8
STONE	1/24	1/20	0/18	2/19	0/25	0/23	1/18	1/42	0/18	0/11	0/11	0/ 7	0/12	0/ 8
HYPERPLASIA	0/24	0/20	0/18	0/19	0/25	2/23	2/18	0/42	0/18	0/11	0/11	0/ 7	0/12	0/ 8
TESTES														
ATROPHY, APLASIA	24/43	24/43	19/39	15/39	26/42	22/41	22/34	46/90	20/37	10/18	13/23	13/19	8/20	10/20
URINARY BLADDER														
HYPERPLASIA (MUCOSA)	0/38	2/41	0/35	0/38	4/42	1/37	1/27	0/83	0/37	0/17	1/21	0/18	0/14	0/17
PROSTATE														
THYMUS														
HYPERPLASIA, EPITHEL	6/20	9/15	5/15	6/20	9/31	12/25	5/16	15/52	8/15	4/10	3/16	4/10	1/ 7	2/ 8
CYST (EPITHELIAL)	8/20	6/15	6/15	8/20	14/31	17/25	9/16	20/52	6/15	6/10	7/16	2/10	6/ 7	3/ 8
CONGESTION	2/20	2/15	2/15	3/20	4/31	4/25	1/16	9/52	2/15	1/10	4/16	3/10	0/ 7	1/ 8
THORACIC LYMPH NODE														
PARTICLES	42/45	42/42	41/42	39/40	44/45	41/42	35/40	1/77	0/35	17/18	24/25	19/20	17/18	20/21
HYPERPLASIA	15/45	5/42	5/42	11/40	6/45	4/42	5/40	18/77	5/35	2/18	1/25	3/20	1/18	4/21
LYMPHOSTASIS	12/45	8/42	7/42	12/40	9/45	12/42	9/40	32/77	9/35	5/18	7/25	5/20	6/18	4/21
GRANULOMA	0/45	0/42	0/42	1/40	0/45	0/42	16/40	0/77	0/35	0/18	0/25	0/20	0/18	0/21
MINERALIZATION	0/45	0/42	0/42	1/40	0/45	0/42	27/40	1/77	0/35	0/18	0/25	0/20	0/18	0/21
CONGESTION	11/45	14/42	11/42	13/40	8/45	10/42	6/40	26/77	12/35	5/18	11/25	8/20	1/18	5/21

LG138

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

ORGAN Lesion	DPOO 5.00	DPFO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCON	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
THORACIC LYMPH NODE +														
HEMORRHAGE	7/45	7/42	1/42	3/40	9/45	5/42	6/40	17/77	7/35	2/18	6/25	1/20	3/18	1/21
BROWN PIGMENT	6/45	0/42	0/42	0/40	2/45	0/42	1/40	29/77	16/35	2/18	2/25	1/20	1/18	1/21
INFLAMMATION	0/45	0/42	2/42	0/40	1/45	0/42	0/40	2/77	1/35	0/18	0/25	0/20	0/18	0/21
FIBROSIS	0/45	0/42	0/42	0/40	0/45	0/42	1/40	1/77	2/35	0/18	0/25	1/20	0/18	2/21
NASAL TURBINATES														
INFLAM. ABSCESS	3/45	5/45	6/44	4/40	2/45	2/42	6/36	8/93	1/42	0/21	0/25	0/22	3/20	4/22
STERNUM BONE MARROW														
SMALL INTESTINE														
INFLAMMATION	6/26	2/23	2/22	1/19	2/35	4/27	2/23	9/50	6/24	1/11	1/ 9	1/10	0/12	1/11
PARASITE	1/26	0/23	0/22	0/19	0/35	0/27	0/23	0/50	0/24	0/11	0/ 9	0/10	0/12	0/11
HEMORRHAGE	0/26	1/23	0/22	0/19	0/35	0/27	0/23	0/50	0/24	0/11	0/ 9	0/10	0/12	0/11
LARGE INTESTINE														
INFLAMMATION	6/30	3/27	6/24	2/21	3/32	3/27	3/22	7/49	6/26	3/12	1/12	1/12	0/12	2/12
INTUSSUSCEPTION	0/30	0/27	1/24	1/21	1/32	2/27	0/22	0/49	0/26	0/12	0/12	1/12	0/12	0/12
STOMACH														
MINERALIZATION	5/38	1/35	4/28	3/29	8/41	1/30	4/26	8/78	3/31	2/20	0/18	0/13	3/13	2/12
HEMORRHAGE	0/38	0/35	0/28	0/29	0/41	3/30	0/26	0/78	0/31	0/20	0/18	0/13	0/13	0/12
MANDIBULAR SG														
MONONUCLE CELL INFIL	2/43	1/44	1/39	4/34	3/46	1/41	3/38	3/88	2/41	0/20	0/23	2/19	2/14	1/19

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

16138

ORGAN Lesion	DPDO 5.00	DPIO 5.00	DEFO 5.00	COFO 5.00	CSFO 5.00	RTFO 5.00	BPFO 2.00	CCUN	DPSV	DPFS	DEFS	COFS	CSFS	RTFS
MANDIBULAR LN														
HYPERPLASIA	29/43	30/41	22/39	22/33	29/44	18/37	20/31	56/83	25/40	16/20	18/21	11/19	7/13	11/17
LYMPHOSTASIS	21/43	18/41	12/39	14/33	20/44	17/37	16/31	39/83	15/40	9/20	6/21	5/19	9/13	7/17
CONGESTION	9/43	6/41	8/39	8/33	12/44	8/37	5/31	15/83	12/40	3/20	3/21	7/19	1/13	6/17
HEMORRHAGE	0/43	1/41	1/39	0/33	1/44	1/37	2/31	3/83	0/40	1/20	1/21	1/19	1/13	0/17
BROWN PIGMENT	4/43	2/41	3/39	2/33	3/44	2/37	3/31	10/83	7/40	4/20	2/21	2/19	1/13	2/17
INFLAMMATION	0/43	1/41	1/39	0/33	0/44	1/37	0/31	2/83	0/40	1/20	0/21	1/19	0/13	0/17
GRANULOMA	0/43	0/41	0/39	0/33	0/44	0/37	3/31	1/83	0/40	0/20	0/21	0/19	0/13	1/17
MINERALIZATION	0/43	0/41	0/39	0/33	0/44	0/37	4/31	0/83	0/40	0/20	0/21	0/19	0/13	1/17
FIBROSIS	1/43	0/41	1/39	0/33	0/44	0/37	0/31	2/83	1/40	0/20	0/21	1/19	0/13	0/17

C.2 Second Replicate - High Dose

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138

ORGAN Lesion	DPOO 5.00	DPFO 05.0	DEFO 05.0	COFO 05.0	CSFO 05.0	RTFO 05.0	BPFO	CCON 0.00	DPSV	DPFS	DEFS	COFS	CSFS	RTFS	GSOO
LUNGS															
PARTICLES	44/44	39/39	48/48	43/43	46/46	40/40	48/48	1/96	1/46	22/22	25/25	21/21	22/22	23/23	1/44
INFLAM REACTION	31/44	30/39	19/48	33/43	10/46	9/40	22/48	2/96	4/46	9/22	14/25	6/21	7/22	10/23	3/44
GRANULOMA	30/44	34/39	20/48	36/43	2/46	16/40	23/48	0/96	0/46	0/22	2/25	1/21	0/22	0/23	0/44
FIBROSIS	8/44	5/39	2/48	14/43	0/46	1/40	4/48	0/96	0/46	0/22	1/25	1/21	1/22	0/23	3/44
HYPERPLASIA ADENO	34/44	24/39	22/48	26/43	17/46	20/40	34/48	26/96	17/46	7/22	13/25	8/21	9/22	9/23	16/44
HYPERPLASIA PAPIL	8/44	3/39	3/48	22/43	3/46	6/40	2/48	0/96	8/46	2/22	0/25	1/21	0/22	3/23	4/44
METAPLASIA, CILIARY	13/44	8/39	3/48	7/43	1/46	0/40	8/48	4/96	1/46	0/22	5/25	0/21	2/22	0/23	0/44
METAPLASIA, SQUAMOUS	2/44	0/39	1/48	20/43	1/46	3/40	1/48	1/96	3/46	2/22	0/25	0/21	0/22	1/23	3/44
PROLIF FIBROBLASTS	2/44	1/39	1/48	5/43	2/46	1/40	2/48	0/96	2/46	1/22	0/25	0/21	0/22	0/23	2/44
MONONUCLE CELL INFIL	25/44	16/39	22/48	18/43	12/46	20/40	20/48	48/96	23/46	14/22	13/25	10/21	11/22	8/23	16/44
CONGESTION	25/44	26/39	34/48	17/43	35/46	22/40	29/48	79/96	34/46	13/22	20/25	13/21	16/22	15/23	30/44
HEMORRHAGE	5/44	1/39	0/48	1/43	1/46	2/40	2/48	9/96	5/46	1/22	1/25	2/21	1/22	3/23	8/44
PNEUMONIA	10/44	13/39	10/48	13/43	17/46	16/40	14/48	50/96	22/46	9/22	6/25	7/21	11/22	11/23	15/44
EMPHYSEMA	24/44	28/39	9/48	19/43	14/46	14/40	13/48	40/96	22/46	12/22	12/25	4/21	12/22	7/23	8/44
PLEURA															
PARTICLES	33/39	28/37	5/45	20/37	5/46	6/40	9/47	0/95	0/46	4/21	4/25	0/18	4/21	1/21	0/46
INFLAM REACTION	9/39	7/37	4/45	6/37	1/46	2/40	9/47	2/95	3/46	1/21	3/25	0/18	1/21	0/21	0/46
FIBROSIS	29/39	23/37	7/45	18/37	3/46	6/40	12/47	4/95	3/46	1/21	2/25	0/18	1/21	0/21	3/46
PROLIFERATION	23/39	16/37	16/45	22/37	8/46	9/40	8/47	30/95	14/46	7/21	9/25	4/18	8/21	6/21	5/46

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138 ORGAN Lesion	DPOO 5.00	DPFO 05.0	DEFO 05.0	COFO 05.0	CSFO 05.0	RTFO 05.0	BPFO	CCON 0.00	DPSV	DPFS	DEFS	COFS	CSFS	RTFS	GSOO
PLEURA *															
MONONUCLE CELL INFIL	5/39	4/37	3/45	1/37	0/46	3/40	3/47	3/95	2/46	0/21	2/25	1/18	2/21	0/21	0/46
PAPILLARY STRUCTURES	12/39	2/37	1/45	1/37	0/46	1/40	0/47	3/95	1/46	0/21	2/25	0/18	0/21	0/21	0/46
LARYNX															
PARTICLES	22/37	29/31	3/38	1/34	2/36	2/31	2/39	1/75	0/36	0/20	1/17	5/18	1/16	4/16	0/42
INFLAM REACTION	1/37	0/31	0/38	0/34	0/36	0/31	0/39	1/75	1/36	1/20	0/17	0/18	1/16	0/16	0/42
ECTASIA (GLANDS)	2/37	1/31	1/38	10/34	3/36	2/31	1/39	7/75	3/36	3/20	2/17	1/18	1/16	3/16	2/42
CYST (GLANDS)	8/37	2/31	5/38	8/34	3/36	4/31	3/39	10/75	7/36	5/20	5/17	4/18	2/16	0/16	10/42
MONONUCLE CELL INFIL	6/37	4/31	8/38	8/34	7/36	8/31	11/39	7/75	5/36	7/20	4/17	3/18	3/16	3/16	6/42
HYPERPLASIA, GLAND	1/37	0/31	0/38	0/34	1/36	0/31	7/39	0/75	2/36	0/20	0/17	0/18	0/16	0/16	1/42
TRACHEA															
PARTICLES	44/44	39/39	7/39	5/35	7/41	5/32	11/39	1/81	0/38	2/18	5/18	9/16	0/14	9/17	0/43
INFLAM REACTION	1/44	1/39	0/39	1/35	0/41	0/32	4/39	1/81	1/38	1/18	0/18	0/16	0/14	0/17	0/43
MONONUCLE CELL INFIL	0/44	7/39	22/39	12/35	9/41	13/32	24/39	8/81	10/38	7/18	5/18	6/16	4/14	4/17	12/43
ECTASIA (GLANDS)	10/44	6/39	8/39	12/35	11/41	6/32	3/39	21/81	11/38	9/18	6/18	4/16	0/14	4/17	6/43
CYSTS (GLANDS)	8/44	2/39	13/39	4/35	5/41	5/32	7/39	20/81	6/38	2/18	5/18	2/16	1/14	3/17	7/43
HYPERPLASIA (MUCOSA)	0/44	0/39	0/39	0/35	0/41	0/32	12/39	0/81	1/38	0/18	0/18	0/16	0/14	0/17	0/43
THYROIDS															
ECTASIA	26/36	24/31	33/44	23/36	22/41	23/35	28/43	75/86	21/40	14/21	17/22	13/18	14/19	11/19	24/43
CYST	12/36	14/31	16/44	11/36	16/41	11/35	14/43	45/86	17/40	10/21	3/22	5/18	5/19	6/19	16/43

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138

ORGAN Lesion	DPOO 5.00	DPFO 05.0	DEFO 05.0	COFO 05.0	CSFO 05.0	RTFO 05.0	BPFO	CCON 0.00	DPSV	DPFS	DEFS	COFS	CSFS	RTFS	GSOO
THYROIDS +															
AMYLOIDOSIS	8/36	5/31	4/44	3/36	3/41	6/35	2/43	8/86	5/40	5/21	3/22	4/18	0/19	2/19	3/43
ATROPHY	0/36	1/31	4/44	0/36	2/41	0/35	3/43	10/86	2/40	2/21	4/22	3/18	0/19	0/19	1/43
PARATHYROIDS															
HYPERPLASIA	1/33	1/26	2/34	1/29	1/33	2/29	2/35	11/77	3/34	0/12	2/18	2/15	1/15	2/15	2/37
ESOPHAGUS															
BRAIN															
CONGESTION	27/31	16/23	32/36	20/25	30/34	21/25	28/35	73/78	25/34	15/19	14/16	13/14	13/18	13/14	29/36
HEMORRHAGE	1/31	1/23	4/36	4/25	3/34	2/25	2/35	7/78	4/34	2/19	1/16	3/14	3/18	1/14	4/36
EDEMA	10/31	9/23	10/36	14/25	11/34	7/25	12/35	28/78	11/34	5/19	9/16	2/14	2/18	5/14	7/36
SPINAL CORD															
CONGESTION	10/29	3/22	11/34	5/27	7/32	5/28	2/35	17/68	6/27	4/16	4/16	2/13	4/15	1/15	3/37
EYES															
CATARACT	7/27	4/17	8/34	4/28	8/36	3/29	6/33	14/64	3/28	3/16	5/13	3/13	2/14	6/15	8/32
FIBROSIS	0/27	1/17	5/34	4/28	6/36	5/29	1/33	6/64	1/28	0/16	0/13	0/13	1/14	1/15	2/32
PITUITARY															
VACUOLIZATION	33/33	19/21	34/34	28/28	31/33	28/29	33/33	70/72	34/34	14/14	14/14	12/13	15/15	14/14	33/35
CYST	3/33	2/21	2/34	1/28	3/33	3/29	2/33	3/72	0/34	2/14	1/14	0/13	0/15	0/14	1/35
CONGESTION	21/33	14/21	23/34	19/28	25/33	25/29	26/33	61/72	22/34	8/14	8/14	10/13	12/15	11/14	24/35
AMYLOIDOSIS	4/33	3/21	1/34	2/28	0/33	2/29	1/33	0/72	7/34	0/14	2/14	2/13	0/15	0/14	4/35

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138

ORGAN Lesion	DPOO 5.00	DPFO 05.0	DEFO 05.0	CDFO 05.0	CSFO 05.0	RTFO 05.0	BPFO	CCON 0.00	DPSV	DPFS	DEFS	CDFS	CSFS	RTFS	GSOO
ADRENAL CORTEX															
HYPERPLASIA	18/37	11/28	29/40	19/33	26/38	24/34	22/40	60/83	27/37	13/21	9/17	9/16	11/17	12/17	22/38
CONGESTION	2/37	4/28	3/40	3/33	2/38	2/34	4/40	9/83	4/37	2/21	0/17	2/16	0/17	1/17	1/38
HEMORRHAGE	23/37	16/28	10/40	16/33	10/38	11/34	13/40	37/83	13/37	8/21	5/17	8/16	6/17	7/17	14/38
BROWN PIGMENT	11/37	6/28	19/40	11/33	9/38	11/34	9/40	30/83	16/37	3/21	6/17	6/16	3/17	9/17	13/38
AMYLOIDOSIS	30/37	22/28	15/40	21/33	18/38	14/34	15/40	39/83	15/37	9/21	10/17	10/16	10/17	10/17	14/38
VACUOLIZATION	2/37	3/28	9/40	4/33	3/38	2/34	2/40	12/83	1/37	3/21	0/17	1/16	1/17	1/17	2/38
ATROPHY	4/37	1/28	4/40	2/33	3/38	0/34	0/40	2/83	3/37	0/21	0/17	0/16	1/17	0/17	1/38
ADRENAL MEDULLA															
CONGESTION	11/36	16/27	18/37	18/28	20/36	23/33	15/36	44/80	15/36	6/13	8/17	4/15	10/15	9/16	13/36
MONONUCLE CELL INFIL	5/36	2/27	8/37	4/28	7/36	8/33	8/36	21/80	9/36	1/19	4/17	5/15	4/15	5/16	10/36
ATROPHY	0/36	0/27	5/37	3/28	1/36	2/33	3/36	7/80	2/36	0/19	1/17	2/15	0/15	1/16	1/36
SPLEEN															
BROWN PIGMENT	19/35	15/28	24/42	28/33	24/40	19/35	31/41	50/88	19/38	13/21	12/19	14/14	6/18	10/18	20/42
FIBROSIS	0/35	1/28	0/42	2/33	3/40	0/35	3/41	4/88	0/38	0/21	1/19	1/14	1/18	0/18	3/42
AMYLOIDOSIS	11/35	13/28	12/42	4/33	14/40	12/35	14/41	31/88	13/38	6/21	5/19	5/14	3/18	4/18	11/42
HYPOPLASIA	4/35	7/28	9/42	1/33	7/40	5/35	7/41	22/88	7/38	3/21	3/19	0/14	3/18	3/18	8/42
HYPERPLASIA	4/35	8/28	8/42	13/33	4/40	9/35	12/41	20/88	5/38	4/21	2/19	3/14	3/18	5/18	9/42
CONGESTION	1/35	0/28	1/42	1/33	4/40	0/35	5/41	8/88	1/38	0/21	1/19	0/14	0/18	0/18	2/42
HEMORRHAGE	0/35	1/28	1/42	2/33	0/40	0/35	3/41	4/88	1/38	0/21	1/19	0/14	0/18	0/18	1/42

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138 ORGAN Lesion	DPOO 5.00	DPFO 05.0	DEFO 05.0	COFO 05.0	CSFO 05.0	RTFO 05.0	BPFO	CCON 0.00	DPSV	DPFS	DEFS	CnFS	CSFS	RTFS	GSOO
PANCREAS															
FATTY INFILTRATION	5/33	6/22	9/36	8/31	6/36	9/30	6/35	20/70	10/33	5/19	6/16	2/16	4/16	1/15	7/36
INFLAMMATION	0/33	0/22	2/36	0/31	4/36	1/30	3/35	6/70	4/33	0/19	2/16	0/16	0/16	1/15	2/36
CYST (DUCTS)	11/33	6/22	2/36	4/31	4/36	6/30	7/35	7/70	5/33	2/19	0/16	4/16	1/16	2/15	3/36
HYPERPLASIA	0/33	1/22	2/36	1/31	0/36	0/30	2/35	3/70	0/33	0/19	0/16	0/16	0/16	1/15	3/36
HEART															
CONGESTION	25/38	21/32	26/47	15/38	21/43	14/39	17/45	55/92	33/44	15/21	15/24	8/20	10/20	7/20	18/32
HEMORRHAGE	5/38	5/32	1/47	3/38	3/43	0/39	0/45	13/92	16/44	0/21	1/24	0/20	1/20	0/20	2/32
INFLAMMATION	11/38	4/32	4/47	6/38	6/43	4/39	7/45	19/92	11/44	8/21	2/24	3/20	3/20	5/20	8/32
FIBROSIS	8/38	1/32	2/47	4/38	2/43	2/39	2/45	8/92	1/44	5/21	1/24	2/20	3/20	2/20	4/32
THROMBOSIS	12/38	7/32	5/47	12/38	7/43	9/39	9/45	23/92	10/44	8/21	3/24	4/20	5/20	7/20	9/32
MINERALIZATION	4/38	5/32	6/47	5/38	6/43	1/39	6/45	11/92	2/44	3/21	6/24	2/20	6/20	5/20	3/32
KIDNEYS															
NEPHROPATHY	38/42	28/36	38/45	34/39	39/42	36/39	41/43	84/93	37/45	19/21	17/20	16/19	16/19	19/19	42/45
NEPHROSCLEROSIS	19/42	17/36	25/45	21/39	26/42	21/39	23/43	51/93	23/45	10/21	12/20	11/19	13/19	15/19	27/45
AMYLOIDOSIS	12/42	10/36	9/45	7/39	12/42	11/39	13/43	26/93	10/45	6/21	5/20	8/19	5/19	3/19	9/45
MINERALIZATION	38/42	34/36	41/45	34/39	32/42	35/39	40/43	74/93	40/45	20/21	18/20	17/19	18/19	17/19	37/45
CONGESTION	10/42	8/36	8/45	8/39	15/42	8/39	10/43	34/93	10/45	9/21	6/20	3/19	5/19	4/19	10/45
MONONUCLE CELL INFIL	4/42	7/36	8/45	2/39	4/42	1/39	4/43	15/93	6/45	5/21	2/20	1/19	2/19	1/19	0/45
INFLAMMATION	0/42	3/36	0/45	2/39	0/42	0/39	1/43	1/93	0/45	0/21	0/20	1/19	0/19	1/19	0/45

L6138

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

ORGAN Lesion	DPOO 5.00	DPFO 05.0	DEFO 05.0	CDFO 05.0	CSFO 05.0	RTFO 05.0	BPFO	CCON 0.00	DPSV	DPFS	DEFS	COFS	CSFS	RTFS	GSOO
LIVER															
CONGESTION	31/39	22/32	23/37	26/34	33/40	27/34	32/39	80/87	29/37	18/21	17/19	11/18	17/19	17/20	34/42
HEMORRHAGE	11/39	8/32	6/37	8/34	9/40	4/34	8/39	13/87	7/37	5/21	2/19	1/18	2/19	3/20	7/42
DEGENERATION, VACUOL	15/39	9/32	7/37	10/34	9/40	10/34	8/39	31/87	13/37	6/21	4/19	6/18	5/19	3/20	7/42
DEGENERATION, GRANUL	17/39	13/32	18/37	11/34	11/40	10/34	17/39	42/87	24/37	6/21	5/19	4/18	8/19	6/20	13/42
NECROSIS	5/39	4/32	0/37	2/34	1/40	0/34	2/39	3/87	4/37	1/21	0/19	0/18	0/19	1/20	1/42
AMYLOIDOSIS	22/39	16/32	12/37	7/34	11/40	14/34	10/39	29/87	13/37	8/21	6/19	11/18	7/19	8/20	11/42
BROWN PIGMENT	31/39	20/32	21/37	19/34	11/40	15/34	21/39	43/87	19/37	14/21	11/19	9/18	10/19	11/20	22/42
INFLAMMATORY CELL	28/39	22/32	32/37	16/34	26/40	19/34	25/39	67/87	27/37	17/21	15/19	12/18	14/19	14/20	26/42
EXTRAMEDUL HEMATOPOL	11/39	7/32	7/37	8/34	7/40	5/34	13/39	25/87	13/37	7/21	6/19	3/18	4/19	4/20	13/42
PARTICLES	0/39	2/32	0/37	0/34	1/40	0/34	1/39	0/87	0/37	2/21	0/19	0/18	0/19	2/20	1/42
PROLIFERATION	22/39	14/32	18/37	4/34	10/40	12/34	13/39	30/87	16/37	7/21	8/19	9/18	6/19	10/20	16/42
CYST	13/39	9/32	12/37	7/34	9/40	11/34	14/39	29/87	15/37	9/21	6/19	6/18	5/19	6/20	18/42
GALL BLADDER															
STONE	2/24	1/15	2/28	1/21	1/23	0/19	0/26	0/48	4/29	1/13	0/10	1/15	0/9	0/12	2/27
TESTES															
ATROPHY, APLASIA	18/39	19/34	17/44	13/39	15/43	16/37	27/44	32/90	16/42	8/20	10/21	5/19	6/18	10/22	16/45
URINARY BLADDER															
HYPERPLASIA (MUCOSA)	0/35	0/26	2/38	0/34	0/36	0/31	0/39	4/74	1/37	1/19	1/17	0/16	3/16	1/17	0/41
PROSTATE															

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138

ORGAN Lesion	DPOO 5.00	DPFO 05.0	DEFO 05.0	COFO 05.0	CSFO 05.0	RTFO 05.0	BPFO	CCON 0.00	DPSV	DPFS	DEFS	COFS	CSFS	RTFS	GSOO
THYMUS															
HYPERPLASIA, EPITHEL	8/28	5/16	11/22	8/20	3/13	13/21	9/16	28/59	15/30	4/15	7/13	6/ 9	2/ 9	3/11	16/26
CYST (EPITHELIAL)	17/28	10/16	15/22	12/20	8/13	11/21	12/16	38/59	18/30	10/15	8/13	7/ 9	4/ 9	6/11	14/26
CONGESTION	0/28	2/16	0/22	2/20	2/13	1/21	0/16	8/59	3/30	1/15	2/13	1/ 9	1/ 9	2/11	6/26
THORACIC LYMPH NODE															
PARTICLES	44/44	35/36	45/45	41/43	37/39	33/34	45/45	2/94	3/33	21/21	20/23	21/21	20/20	22/22	0/32
HYPERPLASIA	2/44	1/36	4/45	8/43	4/39	3/34	12/45	11/94	4/33	2/21	2/23	3/21	2/20	1/22	2/32
LYMPHOSTASIS	14/44	12/36	14/45	13/43	5/39	9/34	14/45	27/94	16/33	5/21	5/23	8/21	5/20	6/22	16/32
GRANULOMA	0/44	0/36	1/45	0/43	0/39	0/34	18/45	0/94	0/33	0/21	0/23	0/21	0/20	0/22	0/32
MINERALIZATION	0/44	0/36	0/45	0/43	0/39	0/34	29/45	1/94	0/33	0/21	0/23	0/21	0/20	0/22	0/32
CONGESTION	9/44	11/36	6/45	7/43	10/39	6/34	4/45	18/94	9/33	6/21	6/23	3/21	2/20	5/22	9/32
HEMORRHAGE	5/44	6/36	2/45	3/43	3/39	3/34	2/45	20/94	4/33	3/21	3/23	1/21	4/20	1/22	5/32
BROWN PIGMENT	0/44	1/36	0/45	0/43	0/39	1/34	1/45	15/94	6/33	0/21	0/23	0/21	0/20	0/22	3/32
NASAL TURBINATES															
CHRONIC INFLAMMATION	7/41	3/39	1/46	2/39	4/45	2/40	4/47	8/99	2/46	1/21	6/24	1/19	0/20	2/21	4/46
STERNUM-BONE MARROW															
SMALL INTESTINE															
INFLAMMATION	1/25	0/19	3/32	3/29	1/26	3/27	1/32	7/61	3/30	0/13	2/12	0/14	0/11	1/15	0/31

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138 ORGAN Lesion	DPOO 5.00	DPFO 05.0	DEFO 05.0	COFO 05.0	CSFO 05.0	RTFO 05.0	BPFO	CCDN 0.00	DPSV	DPFS	DEFS	COFS	CSFS	RTFS	GSOO
LARGE INTESTINE															
INFLAMMATION	3/27	1/17	6/32	5/30	4/30	2/27	3/36	12/63	5/30	1/13	2/15	3/14	1/11	2/15	1/33
STOMACH															
MINERALIZATION	3/34	3/22	0/34	2/33	1/37	2/20	2/35	7/69	5/33	5/17	2/14	1/15	2/13	1/14	1/38
MANDIBULAR SG															
MONONUCLE CELL INFIL	8/39	3/21	5/42	5/37	1/42	4/37	5/42	9/88	6/41	2/21	1/18	3/19	1/19	1/17	1/44
MANDIBULAR LN															
HYPERPLASIA	18/35	10/26	26/42	21/34	10/43	12/35	18/42	49/86	20/39	11/21	8/18	11/17	5/17	11/16	18/41
LYMPHOSTASIS	21/35	14/26	22/42	20/34	19/43	17/35	18/42	38/86	23/39	7/21	7/18	8/17	5/17	8/16	23/41
CONGESTION	8/35	7/26	6/42	10/34	11/43	6/35	8/42	20/86	7/39	5/21	3/18	4/17	2/17	2/16	9/41
HEMORRHAGE	1/35	1/26	0/42	1/34	0/43	1/35	0/42	4/86	1/39	1/21	0/18	0/17	0/17	0/16	1/41
BROWN PIGMENT	2/35	1/26	0/42	0/34	1/43	0/35	0/42	3/86	3/39	0/21	0/18	3/17	1/17	2/16	0/41

C.3 First and Second Replicate - Middle Dose

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138

ORGAN Lesion	DPOO2.5/1	DPFO2.5/1	DEFO2.5/1	COFO2.5/1	CSFO2.5/1	RTFO2.5/1	DPOO2.5/2	DPFO2.5/2	DEFO2.5/2	COFO2.5/2	CSFO2.5/2	RTFO2.5/2
LUNGS												
PARTICLES	43/43	45/45	39/39	45/45	47/47	42/42	47/47	49/49	46/46	45/45	43/43	46/47
INFLAM REACTION	28/43	28/45	11/39	28/45	20/47	7/42	19/47	27/49	7/46	36/45	4/43	14/47
GRANULOMA	14/43	20/45	16/39	39/45	3/47	1/42	9/47	20/49	7/46	44/45	1/43	5/47
FIBROSIS	7/43	6/45	3/39	9/45	3/47	1/42	1/47	8/49	1/46	14/45	0/43	2/47
HYPERPLASIA ADENO	19/43	30/45	17/39	24/45	25/47	12/42	23/47	24/49	14/46	22/45	9/43	23/47
HYPERPLASIA PAPIL	1/43	6/45	3/39	21/45	3/47	2/42	3/47	1/49	2/46	9/45	2/43	2/47
METAPLASIA, CILIARY	4/43	4/45	1/39	3/45	0/47	0/42	4/47	2/49	0/46	5/45	0/43	0/47
METAPLASIA, SQUAMOUS	0/43	2/45	0/39	18/45	2/47	2/42	1/47	2/49	2/46	9/45	2/43	2/47
PROLIF FIBROBLASTS	3/43	4/45	0/39	4/45	2/47	0/42	0/47	3/49	0/46	4/45	0/43	0/47
MONONUCLE CELL INFIL	11/43	15/45	10/39	23/45	22/47	13/42	19/47	13/49	21/46	21/45	11/43	11/47
CONGESTION	31/43	33/45	31/39	23/45	38/47	29/42	28/47	33/49	16/46	26/45	24/43	31/47
HEMORRHAGE	4/43	6/45	3/39	1/45	3/47	4/42	0/47	5/49	1/46	4/45	4/43	1/47
PNEUMONIA	19/43	17/45	11/39	27/45	25/47	18/42	10/47	23/49	20/46	19/45	19/43	22/47
EMPHYSEMA	24/43	25/45	13/39	27/45	32/47	23/42	21/47	38/49	18/46	28/45	21/43	27/47
PLEURA												
PARTICLES	15/40	22/43	7/36	22/41	3/45	6/41	16/45	24/48	6/42	13/41	3/41	5/43
INFLAM REACTION	2/40	3/43	0/36	6/41	0/45	0/41	5/45	7/48	1/42	1/41	0/41	3/43
FIBROSIS	13/40	12/43	5/36	14/41	3/45	2/41	8/45	15/48	4/42	10/41	1/41	4/43
PROLIFERATION	8/40	19/43	12/36	19/41	20/45	12/41	20/45	19/48	16/42	25/41	10/41	16/43

TABLE I
SUMMARY OF GROUP INCIDENCE OF HISTOPATHOLOGIC FINDINGS

L6138

ORGAN Lesion	DPOO2.5/1	DPFO2.5/1	DEFO2.5/1	COFO2.5/1	CSFO2.5/1	RTFO2.5/1	DPOO2.5/2	DPFO2.5/2	DEFO2.5/2	COFO2.5/2	CSFO2.5/2	RTFO2.5/2
PLEURA +												
MONONUCLE CELL INFIL	2/40	3/43	3/36	7/41	1/45	2/41	3/45	1/48	2/42	1/41	0/41	1/43
PAPILLARY STRUCTURES	4/40	2/43	3/36	0/41	1/45	0/41	3/45	3/48	1/42	0/41	0/41	0/43
THORACIC LYMPH NODE												
PARTICLES	42/42	29/32	27/31	43/43	32/35	38/39	30/33	33/35	32/35	40/41	37/37	37/39
HYPERPLASIA	3/42	1/32	2/31	3/43	2/35	1/39	2/33	5/35	0/35	0/41	2/37	1/39
LYMPHOSTASIS	7/42	11/32	9/31	15/43	7/35	10/39	15/33	14/35	17/35	13/41	13/37	12/39
CONGESTION	15/42	5/32	7/31	6/43	9/35	13/39	8/33	11/35	4/35	13/41	13/37	12/39
HEMORRHAGE	3/42	2/32	0/31	6/43	0/35	4/39	0/33	3/35	1/35	3/41	2/37	1/39

APPENDIX D
HISTOPATHOLOGIC INCIDENCE TABLE OF NEOPLASTIC LESIONS

D.1 First Replicate

HISTOPATHOLOGIC INCIDENCE TABLE OF NEOPLASTIC LESIONS FIRST REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
LUNGS																					
Adenoma	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	1/20	----	----	----	----		----
Hemangioma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/22	----		----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	1/42	----	----		1/95
Lymphoma	----	----	----	1/45	1/45	----	----	----	----	----	----	1/22	1/47	----	----	1/44	----	----	----		----
Undifferentiated malignant tumor	----	----	----	1/45	----	----	----	1/39	----	----	----	----	----	----	----	----	----	1/22	1/42		1/95
Adenoacanthoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Malignant adenoacanthoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/44	----	----	----		----
Adenocarcinoma	----	----	----	----	----	----	----	----	----	1/41	----	----	----	----	----	----	----	----	1/42		----
Seminoma, metastatic	----	----	----	----	----	----	1/43	----	----	----	----	----	----	----	----	----	----	----	----		----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Polyp	----	----	----	----	1/45	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
PLEURA																					
Undifferentiated malignant tumor	----	----	----	1/45	----	----	----	1/36	----	----	----	----	----	----	----	----	----	----	----		----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----		----
Mesothelioma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Malignant mesothelioma	----	----	----	----	----	----	1/43	1/36	----	----	----	----	----	----	----	----	----	----	----		----
Lymphoma	----	----	----	----	1/43	----	----	----	----	----	----	----	1/47	----	----	----	----	----	----		----
LARYNX																					
Polyp, papillomatosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/13	----	----	2/20	1/32		1/90
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	1/42	----	----	----	----	----	----		----
TRACHEA																					
Polyp, papillomatosis	3/43	----	----	3/45	----	1/21	----	----	1/21	1/37	----	----	----	----	----	1/35	----	----	5/33		----
Fibroma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/33		----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/33		----
Carcinosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/33		----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	1/43	----	----	----	----	----	----		----
THYROID GLANDS																					
Adenoma	1/43	----	----	1/43	----	----	2/40	----	1/24	1/35	----	----	----	----	----	1/36	----	----	----		5/90
Carcinoma	----	----	----	1/43	----	----	----	----	----	----	----	----	1/43	----	----	----	----	----	----		----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	1/43	----	----	----	----	----	----		----
PARATHYROID GLANDS																					
Adenoma	----	----	1/35	1/32	----	----	----	----	1/21	1/28	----	----	1/39	----	1/12	1/30	----	1/16	2/26		1/72
BRAIN																					
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
FIRST REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
EYE																					
Melanoma	----	----	----	1/26	----	----	----	----	----	----	----	----	----	----	----	1/26	----	----	----		2/59
PITUITARY GLAND																					
Adenoma	1/34	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
ADRENAL CORTEX																					
Carcinoma	3/41	----	2/41	1/41	1/1	1/21	----	1/3	----	2/37	----	----	----	----	3/16	2/37	----	----	1/34		3/83
Adenoma	1/41	----	----	4/41	----	----	----	----	----	1/37	----	----	2/43	1/3	----	2/37	1/1	1/16	----		8/83
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		1/83
Lymphangioma (capsule)	----	----	----	----	----	----	----	1/23	----	----	----	----	----	----	----	----	----	----	----		----
Adrenal medulla	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		1/83
Pheochromacytoma	----	----	----	----	----	----	----	----	1/23	1/37	----	----	----	2/2	----	----	----	----	---		1/83
Neuroblastoma	----	----	----	----	1/1	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
SPLEEN																					
Hemangioma	----	----	----	1/43	----	----	----	----	----	1/33	----	----	----	----	----	----	----	----	----		----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	1/18	----	----	----	----	----	----	----		----
Hemangiosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/36	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
PANCREAS																					
Adenoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/34	----	1/31		2/73
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/31		----
Histocytoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Seminoma, metastatic	----	----	----	----	----	----	----	1/33	----	----	----	----	----	----	----	----	----	----	----		----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		1/73
HEART																					
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Myxomatosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Neoplastic metastases	----	----	----	----	1/2	----	----	----	----	----	----	----	----	----	----	----	----	----	----		1/91
KIDNEYS																					
Adenoma	----	----	----	----	1/2	----	----	----	----	----	----	----	----	----	----	1/41	----	----	----		----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	1/22	----	----	----	----	----	----	----		----
Neoplastic metastases	----	----	1/40	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/41	----	----	----		----

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
FIRST REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
LIVER																					
Hemangioma	----	----	3/38	----	----	----	----	----	----	----	----	----	----	----	1/16	1/34	----	----	----		----
Lymphoma	----	----	----	1/43	----	1/20	----	----	----	----	----	1/19	1/44	----	----	----	----	----	----		----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/34		----
Neoplastic metastases	----	----	1/38	1/43	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/34		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/34	----	----	----		----
GALL BLADDER																					
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/23	----	----	----		----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
TESTES																					
Seminoma	----	----	----	----	----	----	1/39	----	----	----	----	----	----	----	----	----	----	----	----		----
Fibroma	----	----	----	----	----	----	1/39	----	----	----	----	----	----	----	----	----	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
URINARY BLADDER																					
Papillomatosis/papilloma	----	----	----	----	----	----	----	----	1/21	----	----	----	----	----	----	----	----	----	1/27		----
Fibropapilloma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
PROSTATE																					
Neoplasia	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
THYMUS																					
Adenoma	----	----	----	----	----	----	----	1/2	----	2/20	----	----	----	----	----	1/25	----	----	----		----
Adenocarcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		1/52
Thymoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
THORACIC LYMPH NODE																					
Lymphoma	----	----	----	2/42	1/32	1/18	----	----	----	----	----	1/20	1/45	----	----	----	----	----	----		----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	2/45	----	----	----	----	1/21	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	1/35	----	1/42	----	----	----		----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	1/36	----	----	----	----	----	----	----	----	----	----	----		----
NASAL TURBINATES																					
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/20	----	----	----	----		----
SMALL INTESTINE																					
Adenocarcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/11	1/23		----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/27	----	----	----		----

HISTOPATHOLOGIC INCIDENCE TABLE OF NEOPLASTIC LESIONS
FIRST REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
LARGE INTESTINE																					
Adenocarcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/12	----		----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	1/30	----	----	----	----	----	----		----
Hemangioma	----	----	1/26	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Polyp	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/27	----	----	----		----
Mesothelioma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
STOMACH																					
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	1/41	----	----	----	----	----	----		----
MANDIBULAR SALIVARY GLAND																					
Adenoma	----	----	1/41	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Carcinoma	----	----	----	----	----	----	1/39	----	----	----	----	----	----	----	----	----	----	----	----		----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/38		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
MANDIBULAR LYMPH NODE																					
Lymphoma	----	----	----	2/41	----	1/20	----	----	----	----	----	2/19	1/44	----	----	----	----	----	----		----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	1/2	----	1/37	----	----	----		1/83
ABDOMINAL LYMPH NODE																					
Lymphoma	----	----	1/5	1/4	----	1/4	----	----	----	----	----	2/4	----	----	----	----	----	----	1/4		----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	1/4	----	----	1/1	----	----	1/4	1/4		----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	1/4	----	1/5	----	----	----		----
PERIPHERAL LYMPH NODE																					
Lymphoma	----	----	----	----	2/2	1/1	----	----	----	----	----	----	----	----	----	----	----	----	----		----
Seminoma, metastatic	----	----	----	----	----	----	1/2	----	----	----	----	2/7	----	----	----	----	----	----	----		----
CHEEK POUCH																					
Neurilenoma	----	----	----	1/1	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----
SKIN/SUBCUTANEOUS																					
Nervus	----	----	----	----	----	1/5	----	----	----	----	----	----	----	----	----	----	----	----	1/9		----
Melanoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/4	----	----	1/9		----
Sarcoma	----	----	----	----	----	----	----	----	----	----	1/1	----	----	----	----	1/4	----	1/4	----		----
Lymphoma	----	----	----	----	1/7	----	----	----	----	----	----	----	----	----	----	----	----	----	----		----

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
FIRST REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
CONNECTIVE TISSUE/ADIPOSE TISSUE																					
Sarcoma	1/1	----	----	----	----	----	----	----	----	----	----	----	1/3	1/1	----	----	----	----	----		----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	1/2	----	----	----	----	----	----	----	----	1/1	----	----		1/5
Neurofibroma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		1/5
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/1		----
Lymphoma	----	----	----	----	1/1	----	----	----	----	----	----	----	1/3	----	----	----	----	----	----		----
Histocytoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----		1/5
Mesothelioma, malignant	----	----	----	----	----	----	----	1/2	----	----	----	----	----	----	----	----	----	----	----		----
MESENTERY																					
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	1/1	----	----	----	----	----	----	----		----

D.2 Second Replicate

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
SECOND REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe$_2$O$_3$ 5 mg	DP:Fe$_2$O$_3$ 2.5 mg	Solvent + Fe$_2$O$_3$, 5 mg	DE:Fe$_2$O$_3$ 5 mg	DE:Fe$_2$O$_3$ 2.5 mg	Solvent + Fe$_2$O$_3$, 5 mg	COE:Fe$_2$O$_3$ 5 mg	COE:Fe$_2$O$_3$ 2.5 mg	Solvent + Fe$_2$O$_3$, 5 mg	CSC:Fe$_2$O$_3$ 5 mg	CSC:Fe$_2$O$_3$ 2.5 mg	Solvent + Fe$_2$O$_3$, 5 mg	RTE:Fe$_2$O$_3$ 5 mg	RTE:Fe$_2$O$_3$ 2.5 mg	Solvent + Fe$_2$O$_3$, 5 mg	BP:Fe$_2$O$_3$ 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
LUNGS																					
Adenoma	----	----	----	----	1/49	----	1/48	----	----	----	1/45	----	----	----	----	----	----	----	----	----	----
Polyp	----	----	----	1/39	----	----	----	----	----	----	----	----	----	----	----	----	----	----	3/48	----	----
Carcinoma	----	----	----	----	----	----	----	----	----	1/43	1/45	1/21	----	----	----	----	----	----	5/48	----	----
Lymphoma	----	1/47	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	2/96
Neoplastic metastases	----	1/47	----	1/39	----	1/22	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Histofibroma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	1/46	----	----	----	----	----	----	----	----	----	----	----	1/44	----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Seminoma, metastatic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/22	----	----	----	----	----	----
Adenocarcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Hemangioma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
PLEURA																					
Mesothelioma, malignant	----	2/45	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mesothelioma, benign	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	1/42	----	----	----	----	----	----	----	----	----	----	----	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/95
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/21	----	----	----	----	----	----
Myxoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/47	----	----
LARYNX																					
Polyp, papillomatosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/16	----	----	----	3/39	----	----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TRACHEA																					
Polyp, papillomatosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/32	----	----	12/39	----	----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	4/39	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Fibroma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/39	----	----
Carcinosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/39	----	----
THYROID GLANDS																					
Adenoma	----	----	1/40	1/31	----	1/21	----	----	----	----	----	----	----	----	----	----	----	----	----	1/43	1/86
Carcinoma	----	----	----	----	----	----	1/44	----	----	----	----	----	----	----	----	----	----	----	----	2/43	2/86
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
SECOND REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
PARATHYROID GLANDS																					
Adenoma	3/33	----	----	----	----	----	----	----	----	----	----	----	1/33	----	2/15	----	----	----	----	1/37	3/77
BRAIN																					
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/18	----	----	----	----	----	----
EYES																					
Melanoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
PITUITARY GLAND																					
Adenoma	----	----	1/34	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/72
ADRENAL CORTEX																					
Adenoma	2/37	1/1	----	2/28	----	1/21	3/40	2/3	1/17	2/33	----	----	1/38	----	1/17	1/34	----	----	----	4/38	----
Carcinoma	----	----	2/37	----	1/1	1/21	2/40	1/3	----	3/33	1/1	3/16	1/38	----	----	2/34	1/1	----	1/40	1/38	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
ADRENAL MEDULLA																					
Pheochromocytoma	2/36	----	3/36	1/27	----	----	----	----	----	----	----	1/15	1/36	----	----	----	----	----	----	----	----
Neuroblastoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
SPLEEN																					
Hemangioma	2/35	----	----	----	----	----	----	----	----	1/33	3/5	1/14	----	----	----	1/35	----	1/18	----	----	2/88
Lymphoma	----	----	----	----	----	----	----	----	----	1/33	1/5	----	----	----	----	----	----	----	----	----	1/88
Hemangiosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/18	----	----	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/18	----	----	----	----	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
PANCREAS																					
Adenoma	----	----	----	----	----	----	1/36	----	----	----	----	1/16	----	----	----	----	----	----	----	----	----
Neoplastic metastases	----	----	1/33	----	----	----	----	----	1/16	----	----	----	----	----	----	----	----	----	----	----	----
Histocytoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/36	----
Seminoma, metastatic	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Carcinoma, anaplastic	----	----	----	----	----	----	1/36	----	----	----	----	----	----	----	----	----	----	----	----	----	1/70
HEART																					
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/20	----	----	----	----	----	----

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
SECOND REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
KIDNEYS																					
Adenoma	----	----	1/45	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/19	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/39	----	----	----	----	----
LIVER																					
Hemangioma	----	1/13	1/37	----	----	----	----	1/15	----	----	1/12	----	----	----	----	----	----	----	1/39	1/42	1/87
Lymphoma	----	----	----	----	----	----	----	----	----	1/34	----	----	----	----	----	----	----	----	----	----	----
Carcinoma	1/39	1/13	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/87
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/42	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/19	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/34	----	----	----	----	----
GALL BLADDER																					
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	1/21	----	----	----	----	----	----	----	----	----	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/27	----
TESTES																					
Fibroma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Seminoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/18	----	----	----	----	----	----
URINARY BLADDER																					
Papillomatosis	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Fibropapilloma	----	----	----	1/26	----	----	----	----	----	----	----	----	----	----	1/16	----	----	----	----	----	----
PROSTATE																					
Neoplasia	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/21	----	----	----	----	----
THYMUS																					
Adenoma	----	----	----	----	2/17	----	----	----	----	1/20	----	----	1/13	----	----	----	----	----	----	----	----
Adenocarcinoma	----	----	1/30	----	----	----	----	----	----	1/20	1/26	----	----	----	----	----	----	----	1/16	----	1/59
Thynoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/59
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	1/13	----	----	----	1/20	----	----	----	----

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
SECOND REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
THORACIC LYMPH NODE																					
Lymphoma	----	----	----	----	----	----	1/45	----	----	1/43	----	----	----	----	----	----	----	----	1/45	----	1/94
Neoplastic metastases	----	----	1/33	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/45	----	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/20	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	1/35	----	----	----	----	----	----	----	1/34	----	----	----	----	----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/32	----
NASAL TURBINATES																					
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
SMALL INTESTINE																					
Adenocarcinoma	----	----	1/30	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
LARGE INTESTINE																					
Adenocarcinoma	----	----	----	1/17	----	----	1/32	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Hemangioma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mesothelioma	----	----	----	----	----	----	----	----	----	----	1/2	----	----	----	----	----	----	----	----	----	----
Polyp	----	----	----	----	----	----	----	----	----	----	1/2	----	----	----	----	----	----	----	----	----	----
STOMACH																					
Carcinoma	----	----	----	----	----	----	----	----	1/14	----	----	----	----	----	----	----	----	----	----	----	1/69
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
MANDIBULAR SALIVARY GLAND																					
Adenoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/19	----	----	----	----	----	----
MANDIBULAR LYMPH NODE																					
Lymphoma	----	----	----	----	----	----	1/42	----	----	----	----	----	1/43	----	----	----	1/4	----	1/42	1/41	1/86
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/35	----	----	----	1/41	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/17	----	----	----	----	----	----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/41	----
ABDOMINAL LYMPH NODE																					
Lymphoma	----	1/9	----	----	----	----	----	----	----	----	1/3	----	----	----	----	----	1/6	----	1/7	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	1/1	----	----	----	----	----	----	----	----	----	----	----	1/15
Reticulosarcoma	----	----	----	----	----	----	----	1/11	----	----	----	----	----	----	----	----	----	----	----	----	----

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
SECOND REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
SKIN																					
Carcinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	1/1	----	----	----	----	----	----	----
Melanoma	----	1/3	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/3
CONNECTIVE TISSUE/ADIPOSE TISSUE																					
Histocytoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Undifferentiated malignant tumor	----	----	----	1/1	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Neurofibroma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/1	----	----	----	----	----	----
Sarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/5
MESENTERY																					
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Melanoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/1	----	----	----	----
PERIPHERAL LYMPH NODES																					
Lymphoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Neoplastic metastases	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
CHEEK POUCH																					
Neurolinoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Myxoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/1	----	----	----	----	----	----
Lymphoma	----	1/1	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
SKELETAL MUSCLE																					
Reticulosarcoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/1	----	----	----	----	----	----
SEMINAL VESICLES																					
Undifferentiated malignant tumor	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/1	----	----	----	----	----
ECTOPIC TISSUE																					
Adenoma	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/2
MIDDLE EAR																					
Mxyolipsarcoma	----	1/1	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----

HISTOPATHOLOGIC INCIDENCE TABLE
OF NEOPLASTIC LESIONS
SECOND REPLICATE

ORGAN/LESION	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%	Colony Control 0.00
STERNUM																					
Mxyolipsarcoma	----	1/1	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
ABDOMINAL CAVITY																					
Undifferentiated malignant tumor	----	----	----	----	----	----	----	1/1	----	----	----	----	----	----	----	----	----	----	----	----	----

APPENDIX E

GROSS AND HISTOPATHOLOGIC OBSERVATIONS - 12 MONTH SACRIFICE

E.1 Gross Necropsy Observations, First Replicate

GROSS NECROPSY OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg
SKIN	----	----	----	----	----	----	----	----	----	----	----	----	----
MANDIBULAR SALIVARY GLAND													
Enlarged	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5
MANDIBULAR LYMPH NODE													
Enlarged	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5
MAMMARY GLAND	----	----	----	----	----	----	----	----	----	----	----	----	----
STERNUM	----	----	----	----	----	----	----	----	----	----	----	----	----
COSTOCHONDEAL	----	----	----	----	----	----	----	----	----	----	----	----	----
THYMUS	----	----	----	----	----	----	----	----	----	----	----	----	----
THYROID GLAND	----	----	----	----	----	----	----	----	----	----	----	----	----
HEART	----	----	----	----	----	----	----	----	----	----	----	----	----
ESOPHAGUS	----	----	----	----	----	----	----	----	----	----	----	----	----
PARATHYROID	----	----	----	----	----	----	----	----	----	----	----	----	----
LUNG													
Mottled brown	1/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	2/5	0/10	0/10	0/10	1/5
Mottled black	0/20	9/10	9/10	8/10	0/10	9/10	9/10	6/10	1/5	0/10	0/10	0/10	0/5
Mottled grey	0/20	0/10	0/10	0/10	0/10	1/10	0/10	1/10	1/5	0/10	0/10	0/10	0/5
Mottled red	5/20	1/10	1/10	3/10	5/10	4/10	1/10	0/10	0/5	0/10	0/10	0/10	1/5
Nodules	0/20	0/10	0/10	0/10	0/10	0/10	0/10	2/10	0/5	0/10	0/10	0/10	0/5
Tissue mass	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5
Firm	0/20	0/10	1/10	1/10	0/10	1/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5
LARYNX													
Mottled black	0/20	0/10	2/10	0/10	0/10	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5
TRACHEA													
Contained black material	0/20	4/10	2/10	2/10	0/10	3/10	1/10	2/10	0/5	0/10	0/10	0/10	0/5
Frothy fluid	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5
RESPIRATORY LYMPH NODE													
Contained black material	0/20	3/10	2/10	1/10	0/10	0/10	3/10	0/10	0/5	0/10	1/10	0/10	1/5
Enlarged	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5
Red	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5

ORGAN/LESION	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
SKIN	----	----	----	----	----	----	----	----	----	----	----	----	----	
MANDIBULAR SALIVARY GLAND														
Enlarged	0/10	0/10	1/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
MANDIBULAR LYMPH NODE														
Enlarged	0/10	0/10	1/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
MAMMARY GLAND	----	----	----	----	----	----	----	----	----	----	----	----	----	
STERNUM	----	----	----	----	----	----	----	----	----	----	----	----	----	
COSTOCHONDEAL	----	----	----	----	----	----	----	----	----	----	----	----	----	
THYMUS	----	----	----	----	----	----	----	----	----	----	----	----	----	
THYROID GLAND	----	----	----	----	----	----	----	----	----	----	----	----	----	
HEART	----	----	----	----	----	----	----	----	----	----	----	----	----	
ESOPHAGUS	----	----	----	----	----	----	----	----	----	----	----	----	----	
PARATHYROID	----	----	----	----	----	----	----	----	----	----	----	----	----	
LUNG														
Mottled brown	4/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	4/10	
Mottled black	2/10	6/10	0/10	0/5	0/10	0/10	1/10	0/5	1/10	1/10	0/10	0/5	0/10	
Mottled grey	1/10	1/10	0/10	1/5	0/10	0/10	1/10	0/5	0/10	0/10	0/10	0/5	0/10	
Mottled red	2/10	2/10	4/10	0/5	4/10	3/10	1/10	1/5	5/10	4/10	3/10	2/5	2/10	
Nodules	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Tissue mass	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Firm	1/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
LARYNX														
Mottled black	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
TRACHEA														
Contained black material	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Frothy fluid	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
RESPIRATORY LYMPH NODE														
Contained black material	0/10	0/10	1/10	0/5	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Enlarged	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Red	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	

GROSS NECROPSY OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
LIVER																											
Granular	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	2/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	
Tan/pale foci	0/20	1/10	1/10	0/10	1/10	0/10	0/10	0/10	0/5	1/10	1/10	0/10	0/5	0/10	0/10	1/10	1/5	1/10	0/10	0/10	0/5	1/10	0/10	1/10	1/5	2/10	
Mottled red	1/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	1/10	0/10	0/10	0/5	0/10	0/10	0/10	1/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Black focus	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	1/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	1/10	0/10	0/5	0/10	
GALL BLADDER																											
Contained black fluid	0/20	0/10	0/10	1/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	1/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Aplasia	0/20	0/10	0/10	0/10	1/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
ADRENAL GLANDS																											
Tan	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	1/5	0/10	0/10	1/10	0/5	0/10	1/10	0/10	0/5	0/10	
Focal adhesions	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Enlarged	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	1/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Pitted	0/20	0/10	0/10	0/10	0/10	0/10	0/10	1/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Red foci	0/20	0/10	0/10	0/10	0/10	0/10	0/10	1/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Firm	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
SPLEEN																											
Dard red	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	1/10	0/10	0/10	0/5	0/10	0/10	0/10	1/5	0/10	0/10	1/10	0/5	0/10	0/10	0/10	0/5	2/10	
Enlarged	0/20	0/10	1/10	0/10	0/10	0/10	0/10	0/10	0/5	1/10	0/10	0/10	0/5	0/10	0/10	0/10	1/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	
Nodule	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	0/10	0/10	0/5	1/10	
Small	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	0/10	0/10	0/5	0/10	
Accessory	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	0/10	0/10	0/5	0/10	
PANCREAS	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
KIDNEY																											
Granular/pitted	0/20	0/10	1/10	0/10	1/10	0/10	0/10	0/10	1/5	1/10	4/10	0/10	0/5	0/10	2/10	1/10	1/5	0/10	2/10	2/10	1/5	0/10	1/10	1/10	0/5	1/10	
Pale/tan, diffuse	1/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	1/5	1/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	1/10	2/10	0/5	0/10	1/10	1/10	0/5	1/10	
Mottled	1/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	1/10	1/10	0/5	0/10	1/10	1/10	0/5	0/10	
Tan focus	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Tissue mass	0/20	0/10	1/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
URINARY BLADDER																											
Blood filled	0/20	0/10	0/10	1/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Concretions	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	1/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	
TESTES																											
Small	0/20	2/10	0/10	0/10	1/10	0/10	0/10	0/10	0/5	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	3/10	1/10	0/10	1/5	0/10	
EPIDIDYMIS																											
Small	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	0/10	0/10	0/5	0/10	
SEMINAL VESICLE																											
Mass	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	1/10	0/10	0/5	0/10	

GROSS NECROPSY OBSERVATIONS

FIRST REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
PROSTATE	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
STOMACH																											
Edema	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
DUODENUM	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
JEJUNUM	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
ILEUM	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
CECUM																											
Blood filled	0/20	0/10	0/10	1/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Enlarged/bloated	0/20	0/10	0/10	0/10	0/10	0/10	2/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Firm	0/20	0/10	0/10	0/10	0/10	0/10	2/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
RECTUM																											
Blood filled	0/20	0/10	0/10	1/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
MESENTERY LYMPH NODE																											
Enlarged	0/20	0/10	0/10	0/10	0/10	1/10	1/10	1/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	1/10	0/10	0/10	0/5	1/10	0/10	2/10	0/5	0/10	
Tan/pale	0/20	0/10	0/10	0/10	0/10	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
SKELETAL MUSCLE	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
EAR	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
EYE																											
Small	0/20	0/10	0/10	1/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Missing	0/20	0/10	1/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	1/10	0/5	0/10	
NASAL TURBINATE	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
BRAIN	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
SPINAL CORD																											
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
BONE (FEMUR)	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
PITUITARY GLAND	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	
COLON																											
Enlarged/bloated	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	2/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Blood filled	0/20	0/10	0/10	1/10	0/10	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	
Firm	0/20	0/10	0/10	0/10	0/10	0/10	0/10	0/10	0/5	0/10	1/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	0/10	0/10	0/5	0/10	

E.2 Gross Necropsy Observations, Second Replicate

GROSS NECROPSY OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3, 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
LUNGS																											
Mottled brown	1/20	----	----	1/10	----	----	----	----	2/5	1/10	----	1/10	----	3/10	3/10	3/10	----	1/10	3/10	2/10	2/5	1/10	2/10	----	----	----	1/10
Mottled black	----	10/10	9/10	7/10	----	10/10	10/10	10/10	1/5	3/10	----	----	2/5	3/10	4/10	----	----	2/10	----	----	----	----	----	----	1/5	----	----
Mottled grey	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled red	6/20	----	3/10	4/10	3/10	2/10	2/10	6/10	1/5	2/10	5/10	1/10	3/5	6/10	5/10	5/10	1/5	3/10	2/10	4/10	1/5	4/10	2/10	1/10	3/5	3/10	3/10
LARYNX																											
Mottled black	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
TRACHEA																											
Contained black material	----	6/10	4/10	1/10	----	5/10	4/10	3/10	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
RESPIRATORY LYMPH NODE																											
Contained black material	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
STERNUM																											
Mass	1/20	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
HEART																											
Mottled black	----	----	1/10	3/10	----	1/10	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
THYMUS																											
Mottled black	----	----	----	----	----	1/10	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
SPLEEN																											
Dark red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Enlarged	----	----	----	1/10	----	----	1/10	----	----	----	----	----	----	1/10	----	----	----	----	1/10	----	----	----	1/10	----	----	----	----
Nodule (white)	----	----	----	----	----	----	----	----	----	----	----	----	1/5	----	----	----	----	----	----	----	----	----	----	----	----	----	----
LIVER																											
Granular	----	1/10	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Mottled red	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	1/10	----	----	----	----	----	----	----	1/10	----	----	----	----
Dark brown	----	1/10	----	1/10	----	2/10	2/10	----	----	----	1/10	1/10	----	1/10	1/10	----	----	----	1/10	----	----	----	----	----	----	1/10	1/10
Tan focus	----	1/10	----	----	----	----	----	1/10	----	1/10	----	----	----	----	----	1/10	----	----	----	1/10	----	1/10	1/10	----	1/5	----	----
Cystic	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----
Mottled black	----	----	----	----	----	----	----	1/10	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----
KIDNEY																											
Granular/pitted	1/20	----	1/10	2/10	1/10	1/10	1/10	2/10	----	----	1/10	2/10	----	2/10	----	----	----	----	3/10	----	1/5	2/10	1/10	----	----	----	----
Tan, diffuse	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	1/10	----	----	----	----	----	----	----	----	----	----	----
Tan, focus	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10
Mottled red	1/20	----	----	----	----	----	----	----	----	----	1/10	----	----	1/10	1/10	----	----	----	----	----	----	----	----	----	----	----	----
ADRENAL GLAND																											
Tan	----	----	----	----	----	1/10	----	----	----	----	----	----	1/5	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----
Pitted	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----

GROSS NECROPSY OBSERVATIONS

SECOND REPLICATE

ORGAN/LESION	Colony Control 0.00	Diesel Particle 5 mg	Diesel Particle 2.5 mg	Diesel Particle 1.25 mg	Solvent 0.00	DP:Fe_2O_3 5 mg	DP:Fe_2O_3 2.5 mg	DP:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	DE:Fe_2O_3 5 mg	DE:Fe_2O_3 2.5 mg	DE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	COE:Fe_2O_3 5 mg	COE:Fe_2O_3 2.5 mg	COE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	CSC:Fe_2O_3 5 mg	CSC:Fe_2O_3 2.5 mg	CSC:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	RTE:Fe_2O_3 5 mg	RTE:Fe_2O_3 2.5 mg	RTE:Fe_2O_3 1.25 mg	Solvent + Fe_2O_3, 5 mg	BP:Fe_2O_3 2 mg	Gelatin Saline 0.5%
ADRENAL GLAND (contd)																											
Enlarged	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10
Mottled red	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10
White focus	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----
MESENTERIC LYMPH NODE																											
Enlarged	2/20	----	----	1/10	----	2/10	1/10	----	----	----	----	2/10	1/5	1/10	1/10	----	----	----	1/10	----	----	3/10	1/10	----	----	----	1/10
STOMACH																											
Edema	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----
CECUM																											
Enlarged	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	1/10	----	----	----	1/10	----	----	----	----
Mass	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
Firm	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	1/10	----	----	----	----
COLON																											
Firm	----	----	----	----	----	----	----	----	----	1/10	----	----	----	1/10	----	----	----	----	----	----	----	----	1/10	----	----	----	----
RECTUM																											
Firm	----	----	----	----	----	----	----	----	----	1/10	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----
TESTES																											
Small	1/20	----	3/10	----	1/10	----	----	1/10	----	----	2/10	----	----	1/10	----	----	----	2/10	2/10	----	1/5	1/10	----	----	----	----	----
Dark red	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----
EPIDIDYMIS																											
Small	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	1/10	1/10	----	----	1/10	----	----	----	----	----
SEMINAL VESICLE																											
Small	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----
PROSTATE																											
Small	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----
SPINAL COLUMN																											
Mottled black	----	----	1/10	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----
EYES																											
Crusty	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----
ABDOMINAL ORGANS																											
Adhesions	----	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----
MANDIBULAR SALIVARY GLAND																											
Mass	----	----	----	----	----	----	----	----	----	----	----	----	----	----	1/10	----	----	----	----	----	----	----	----	----	----	----	----

E.3 Histopathology Summary Table, First Replicate

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 1

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control
LUNGS																										
Particles	10/10	9/9	10/10	–	10/10	9/9	10/10	5/5	10/10	9/9	9/9	5/5	10/10	9/9	9/9	5/5	10/10	10/10	9/9	5/5	10/10	9/9	10/10	5/5	10/10	–
Inflammatory Reaction	10/10	9/9	7/10	2/10	10/10	6/9	7/10	4/5	5/10	5/9	1/9	4/5	9/10	9/9	8/9	4/5	3/10	6/10	2/9	1/5	7/10	5/9	8/10	2/5	5/10	1/20
Granuloma	10/10	8/9	4/10	–	10/10	5/9	4/10	–	7/10	7/9	4/9	1/5	10/10	9/9	9/9	1/5	3/10	1/10	–	–	2/10	2/9	–	1/5	2/10	–
Fibrosis	6/10	2/9	2/10	–	10/10	1/9	–	–	–	1/9	–	–	7/10	1/9	–	–	2/10	–	–	–	1/10	–	–	–	–	1/20
Hyperplasia, Adenomatous	10/10	9/9	7/10	5/10	10/10	8/9	9/10	4/5	6/10	5/9	4/9	4/5	9/10	9/9	6/9	5/5	5/10	6/10	8/9	4/5	8/10	5/9	8/10	5/5	5/10	6/20
Hyperplasia, Papillary	10/10	4/9	–	–	10/10	6/9	5/10	1/5	4/10	2/9	1/9	–	8/10	6/9	3/9	–	–	2/10	2/9	–	2/10	2/9	1/10	–	–	–
Metaplasia, Ciliary	8/10	2/9	3/10	–	10/10	1/9	2/10	–	1/10	–	3/9	–	6/10	3/9	2/9	–	1/10	4/10	1/9	–	4/10	2/9	1/10	–	–	–
Metaplasia, Squamous	1/10	–	–	–	–	–	–	–	–	–	–	–	5/10	5/9	2/9	–	–	–	–	–	–	2/9	–	–	–	–
Adenoma	2/10	–	–	–	1/10	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mononuclear Cell Infiltrate	8/10	8/10	8/10	9/10	7/10	5/9	8/10	4/5	8/10	9/9	1/9	3/5	5/10	7/9	7/9	5/5	6/10	9/10	7/9	2/5	7/10	8/9	7/10	3/5	7/10	7/20
Congestion	7/10	7/9	5/10	3/10	5/10	4/9	6/10	3/5	7/10	6/9	5/9	1/5	9/10	6/9	7/9	3/5	8/10	7/10	9/9	1/5	9/10	7/9	7/10	4/5	1/10	3/20
Hemorrhage	5/10	1/9	3/10	–	3/10	1/9	1/10	–	4/10	1/9	–	–	–	2/9	2/9	1/5	2/10	1/10	2/9	–	1/10	1/9	1/10	–	–	1/20
Pneumonia	4/10	4/9	2/10	1/10	5/10	–	1/10	2/5	4/10	1/9	1/9	–	4/10	6/9	3/9	–	1/10	5/10	6/9	–	–	–	3/10	1/5	–	–
Emphysema	8/10	3/9	2/10	1/10	2/10	1/9	1/10	2/5	4/10	2/9	–	–	6/10	5/9	4/9	1/5	3/10	6/10	8/9	1/5	1/10	1/9	2/10	1/5	–	–
Brown Pigment	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Foreign Body	–	–	–	2/10	–	–	3/10	–	–	1/9	1/9	–	1/10	–	–	–	–	–	–	–	1/10	–	1/10	–	–	3/20
Atelectasis	–	–	1/10	–	1/10	–	–	–	1/10	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–
Polyp	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Edema	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	1/10	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 1

ORGAN Lesion	Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control
PLEURA																											
Particles		3/10	3/9	1/10	–	6/10	3/9	–	–	–	–	–	1/5	3/10	1/9	–	–	1/10	–	–	–	–	–	–	–	1/10	–
Inflammatory Reaction		7/10	8/9	3/10	–	2/10	2/9	3/10	1/5	1/10	–	1/9	1/5	6/10	1/9	1/9	2/5	1/10	–	–	–	–	–	–	–	1/10	–
Fibrosis		1/10	3/9	2/10	–	9/10	1/9	–	–	1/10	–	–	–	2/10	1/9	5/9	–	1/10	–	–	–	–	–	–	–	–	–
Proliferation		–	–	–	–	3/10	1/9	–	–	–	–	–	–	1/10	–	–	–	1/10	–	–	–	–	–	–	–	–	–
Hyperplasia		–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mononuclear Cell Infiltrate		–	–	–	–	–	–	–	–	–	–	–	–	3/10	–	–	–	–	–	1/9	–	–	–	–	–	–	–
Edema		–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–
LARYNX																											
Particles		4/10	3/9	–	–	5/10	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	1/5	–	–	–	–	1/10	–
Inflammatory Reaction		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–
Mononuclear Cell Infiltrate		–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Ectasia		–	–	–	–	–	–	–	–	–	–	2/9	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–
Polyp		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–
Cysts		–	–	–	–	–	–	–	–	–	1/9	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Submucosal Gland-Cyst		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 1

ORGAN Lesion	Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control
TRACHEA																											
Particles		9/10	8/9	7/10	–	8/10	4/9	9/10	–	4/10	3/9	–	1/5	7/10	2/9	–	3/5	1/10	–	–	1/5	–	–	–	–	3/10	–
Inflammatory Reaction		–	–	1/10	–	–	–	–	–	–	1/9	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	1/10	–
Hyperplasia		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	1/10	–
Hyperplasia, Papillary		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–
Metaplasia		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–
Submucosal Gland-Ectasia		–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	1/10	3/20
Submucosal Gland-Cysts		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	1/10	–	–	–
THYROIDS																											
Ectasia		9/10	9/10	9/10	10/10	10/10	9/9	9/10	5/5	9/10	8/9	8/9	5/5	9/10	9/9	6/9	5/5	8/10	10/10	9/9	5/5	5/10	9/9	8/10	5/5	10/10	15/20
Cysts		5/10	6/9	5/10	6/10	3/10	2/9	2/10	2/5	2/10	3/9	4/9	3/5	3/10	1/9	5/9	1/5	3/10	7/10	4/9	4/5	1/10	3/9	6/10	1/5	–	1/20
Proliferation		–	–	–	–	–	1/9	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Amyloidosis		–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	–	–
Fatty Infiltration		–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–
Degeneration, Vacuolar		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–
Congestion		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–

HISTOPATHOLOGY SUMMARY TABLE

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Male Syrian Hamsters
Replicate 1

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control
PARATHYROIDS																										
Hyperplasia	1/10	–	–	–	1/10	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–
ESOPHAGUS																										
Hyperplasia	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Edema	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20
BRAIN																										
Congestion	7/10	6/9	7/10	5/10	5/10	6/9	3/10	3/5	6/10	6/9	5/9	2/5	9/10	7/9	3/9	3/5	5/10	7/10	6/9	4/5	6/10	5/9	8/10	3/5	–	3/20
Edema	4/10	2/9	2/10	3/10	2/10	3/9	2/10	1/5	2/10	5/9	6/9	2/5	3/10	7/9	2/9	2/5	4/10	5/10	3/9	1/5	5/10	2/9	1/10	3/5	2/10	6/20
Hemorrhage	–	1/9	–	–	2/10	1/9	–	–	–	2/9	–	–	2/10	1/9	–	–	1/10	2/10	3/9	–	–	1/9	1/10	–	–	–
Mineralization	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	1/9	–	–	–	–	–	1/10	–	–	–	–	–
Mononuclear Cell Infiltrate	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–
Fibrosis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–
SPINAL CORD																										
Congestion	1/10	–	1/10	1/10	–	1/9	–	–	–	2/9	–	–	1/10	1/9	–	–	1/10	1/10	–	–	1/10	–	–	–	–	1/20
Hemorrhage	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

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Male Syrian Hamsters
Replicate 1

ORGAN Lesion	Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control
EYES																											
Melanoma		–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–
PITUITARY																											
Vacuolization		5/10	3/9	6/10	3/10	8/10	5/9	6/10	4/5	4/10	5/9	8/9	4/5	8/10	8/9	8/9	2/5	8/10	10/10	9/9	3/5	10/10	8/9	7/10	3/5	1/10	9/20
Congestion		1/10	2/9	–	–	1/10	–	–	–	–	–	1/9	–	–	5/9	1/9	1/5	2/10	3/10	5/9	–	3/10	3/9	2/10	–	1/10	2/20
Hemorrhage		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–
Mineralization		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	1/20
Cyst(s)		–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	2/10	–	–	–	–	–	–	–	–	–
ADRENAL CORTEX																											
Hyperplasia		6/10	4/9	6/10	3/10	5/10	7/9	4/10	1/5	7/10	4/9	5/9	2/5	9/10	6/9	6/9	1/5	3/10	5/10	3/9	2/5	6/10	5/9	4/10	3/5	2/10	7/20
Adenoma		–	–	1/10	–	–	1/9	–	–	–	–	–	–	2/10	–	1/9	–	–	–	1/9	1/5	–	1/9	–	–	1/10	–
Brown Pigment		5/10	1/9	–	1/10	2/10	1/9	4/10	2/5	5/10	4/9	6/9	3/5	5/10	2/9	3/9	–	1/10	1/10	3/9	–	4/10	2/9	3/10	3/5	1/10	1/20
Amyloidosis		1/10	1/9	–	2/10	2/10	–	1/10	2/5	1/10	2/9	–	1/5	4/10	3/9	3/9	1/5	–	2/10	1/9	–	2/10	1/9	–	–	–	5/20
Hemorrhage		–	–	–	1/10	1/10	–	1/10	1/5	–	–	–	–	2/10	2/9	1/9	–	–	–	–	–	–	–	–	–	–	1/20
Congestion		–	–	–	–	1/10	–	–	–	–	1/9	–	–	4/10	1/9	–	–	–	–	–	–	1/10	–	–	–	–	–
Mononuclear Cell Infiltrate		–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–
Carcinoma		–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–
Cyst		–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

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Male Syrian Hamsters
Replicate 1

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control
ADRENAL CORTEX (contd)																										
Hypertrophy	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–
ADRENAL MEDULLA																										
Congestion	–	–	–	–	–	–	–	1/5	–	2/9	–	–	5/10	–	1/9	–	–	1/10	1/9	–	1/10	–	–	–	–	–
Amyloidosis	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–
Brown Pigment	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–
SPLEEN																										
Fibrosis	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–
Amyloidosis	–	1/9	–	1/10	1/10	–	–	–	2/10	1/9	–	–	–	–	–	1/5	–	2/10	1/9	–	–	1/9	–	–	–	–
Congestion	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–
Hyperplasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–
Hemorrhage	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–
Hemangioma	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–
Vessels-Ectasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–
PANCREAS																										
Cysts	–	–	2/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mononuclear Cell Infiltrate	–	–	1/10	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

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Male Syrian Hamsters
Replicate 1

ORGAN Lesion Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control
PANCREAS (contd)																										
Hyperplasia	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Fatty Infiltration	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	1/5	–	–	–	–	–	–	1/10	–	–	–
Peripancreatitis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–
Ducts-Ectasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–
Duct-Retention	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–
Capsule-Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–
HEART																										
Congestion	4/10	7/9	4/10	5/10	7/10	1/9	6/10	1/5	5/10	9/9	7/9	–	8/10	5/9	6/9	2/5	5/10	7/10	7/9	1/5	7/10	6/9	8/10	3/5	2/10	5/20
Inflammation	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Hemorrhage	–	–	2/10	2/10	2/10	–	3/10	1/5	3/10	4/9	1/9	–	5/10	2/9	1/9	–	2/10	1/10	1/9	–	1/10	2/9	1/10	–	–	–
KIDNEYS																										
Nephropathy	10/10	9/9	10/10	10/10	10/10	9/9	10/10	5/5	10/10	9/9	9/9	5/5	9/10	9/9	8/9	4/5	10/10	10/10	9/9	5/5	10/10	9/9	10/10	5/5	10/10	20/20
Nephrosclerosis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–
Amyloidosis	–	1/9	–	1/10	1/10	–	–	–	1/10	–	–	–	–	–	1/9	1/5	–	–	1/9	–	–	1/9	–	–	–	–
Mineralization	8/10	8/9	10/10	8/10	6/10	8/9	7/10	5/5	9/10	9/9	7/9	5/5	9/10	9/9	5/9	3/5	9/10	8/10	7/9	5/5	9/10	7/9	10/10	5/5	4/10	10/20
Congestion	5/10	2/9	–	2/10	–	1/9	4/10	2/5	3/10	3/9	–	2/5	5/10	3/9	2/9	1/5	2/10	2/10	2/9	2/5	1/10	–	2/10	1/5	1/10	2/20
Adenoma	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

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Male Syrian Hamsters
Replicate 1

ORGAN Lesion Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control
KIDNEYS (contd)																										
Hemangioendothelioma, Metastasis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–
LIVER																										
Congestion	6/10	6/9	9/10	7/10	7/10	9/9	9/10	3/5	10/10	8/9	6/9	3/5	7/10	8/9	6/9	3/5	7/10	8/10	9/9	3/5	9/10	5/9	10/10	4/5	7/10	15/20
Hemorrhage	–	2/9	2/10	–	–	1/9	–	–	–	–	–	–	–	1/9	–	–	1/10	–	–	–	–	–	1/10	–	–	–
Degeneration, Vacuolar	10/10	8/9	8/10	7/10	9/10	6/9	9/10	4/5	8/10	6/9	5/9	3/5	7/10	5/9	4/9	4/5	7/10	7/10	5/9	4/5	5/10	3/9	6/10	4/5	6/10	13/20
Degeneration, Granular	4/10	3/9	4/10	3/10	4/10	4/9	3/10	3/5	5/10	2/9	3/9	4/5	9/10	4/9	6/9	2/5	6/10	7/10	6/9	4/5	5/10	7/9	6/10	1/5	3/10	6/20
Amyloidosis	–	1/9	–	2/10	1/10	–	–	1/5	1/10	1/9	1/9	–	–	1/9	–	1/5	–	2/10	1/9	–	1/10	1/9	–	–	–	3/20
Brown Pigment	–	1/9	1/10	–	2/10	–	–	–	2/10	–	2/9	1/5	–	–	1/9	1/5	–	2/10	–	–	–	1/9	–	–	1/10	2/20
Extramedullary Hematopoiesis	1/10	1/9	–	–	1/10	–	2/10	–	–	–	1/9	–	–	2/9	–	–	–	1/10	–	–	–	1/9	–	–	–	1/20
Proliferation, Bile Duct	–	–	–	2/10	2/10	–	1/10	1/5	–	1/9	1/9	–	1/10	–	–	1/5	–	2/10	1/9	–	1/10	1/9	–	–	–	–
Mononuclear Cell Infiltrate	1/10	1/9	1/10	1/10	2/10	1/9	–	–	–	1/9	2/9	1/5	–	–	–	–	–	–	1/9	–	–	–	–	–	1/10	–
Dilatation, Bile Duct	–	–	–	–	1/10	–	–	–	–	–	1/9	–	–	1/9	–	1/5	–	1/10	–	–	1/10	–	–	–	1/10	–
Hepatitis	2/10	2/9	4/10	2/10	4/10	5/9	9/10	2/5	10/10	6/9	4/9	1/5	7/10	8/9	7/9	3/5	5/10	7/10	9/9	3/5	9/10	6/9	8/10	4/5	4/10	12/20
Granuloma	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mineralization	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–
Ectasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

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Male Syrian Hamsters
Replicate 1

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control
LIVER (contd)																										
Kupffer Cell Proliferation	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Kupffer Cells-Pigment	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–
Abscess	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–
Necrosis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	3/20	–
Fibrosis	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
GALL BLADDER																										
Stone	–	1/9	1/10	–	–	1/9	–	–	–	–	–	–	–	–	1/9	–	1/10	–	–	1/5	–	1/9	–	–	–	–
Cyst	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–
Papillomatosis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	–	–
Atrophy	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20	–
Necrosis	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
TESTES																										
Atrophy	1/10	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–
Hypospermia	2/10	–	–	–	–	–	–	1/5	–	1/9	–	–	2/10	–	1/9	–	–	–	–	–	4/10	4/9	–	1/5	1/10	–
Degeneration	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mineralization	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	1/5	–	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 1

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control
SEMINAL VESICLES																										
Mineralization	–	–	–	–	–	1/9	–	–	1/10	–	–	–	–	1/9	–	–	–	1/10	–	–	–	1/9	–	1/5	–	–
Hemangioendothelioma	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–
URINARY BLADDER																										
Hyperplasia	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Polyp	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Edema	–	–	–	1/10	–	–	1/10	–	1/10	1/9	2/9	–	–	1/9	2/9	–	1/10	2/10	1/9	–	3/10	1/9	–	–	–	1/20
Giant Cell Formation	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	1/10	1/10	1/9	–	3/10	–	–	–	–	–
Fibropapilloma	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–
PROSTATE	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
THYMUS																										
Cyst	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mineralization	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Hyperplasia (Epithelial)	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–
Congestion	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	1/10	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 1

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control
THORACIC LYMPH NODE																										
Particles	10/10	8/9	9/10	–	10/10	9/9	10/10	4/5	10/10	9/9	8/9	5/5	9/10	9/9	9/9	4/5	8/10	10/10	9/9	5/5	10/10	9/9	10/10	5/5	10/10	1/20
Hyperplasia	7/10	8/9	5/10	3/10	6/10	4/9	3/10	3/5	1/10	5/9	2/9	3/5	5/10	3/9	–	4/5	1/10	3/10	–	4/5	4/10	1/9	1/10	1/5	7/10	1/20
Lymphostasis/Edema	1/10	–	1/10	4/10	–	–	1/10	–	–	1/9	–	–	1/10	–	–	–	–	–	1/9	–	1/10	2/9	–	2/5	–	1/20
Hemorrhage	3/10	–	–	3/10	–	–	–	–	1/10	1/9	–	1/5	1/10	–	1/9	1/5	–	–	–	–	1/10	–	1/10	–	3/10	2/20
Congestion	–	–	–	1/10	–	–	–	–	–	2/9	–	–	–	–	1/9	–	–	1/10	–	–	–	1/9	1/10	–	–	–
Brown Pigment	–	–	–	2/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20
Granuloma	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	6/10	–
NASAL TURBINATES	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
STERNUM (BONE MARROW)	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
SMALL INTESTINE																										
Inflammation	–	–	–	1/10	–	–	–	–	1/10	–	–	–	–	–	3/9	–	1/10	1/10	–	–	–	–	–	–	–	–
LARGE INTESTINE																										
Inflammation	–	–	–	–	–	–	–	–	1/10	3/9	–	–	1/10	1/9	–	2/5	1/10	1/10	–	–	1/10	1/9	1/10	–	–	1/20
Mineralization	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Granuloma	–	–	–	–	–	1/9	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 1

ORGAN Lesion Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control
LARGE INTESTINE (contd)																										
Ulcer	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	–	–
Parasite	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20
Foreign Body	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	–	–
STOMACH																										
Hyperplasia	1/10	–	–	3/10	–	–	–	–	–	–	–	–	–	–	1/9	1/5	–	–	–	–	–	–	–	–	1/10	1/20
Mineralization	–	–	–	–	–	–	1/10	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2/20
Fibropapilloma	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	–	–
Squamous Cell Carcinoma	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Ulcer	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	1/20
Acanthosis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–
Hyperkeratosis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–
MANDIBULAR LYMPH NODE																										
Hyperplasia	10/10	9/9	10/10	10/10	8/10	7/9	9/10	5/5	9/10	8/9	9/9	5/5	9/10	8/9	7/9	4/5	10/10	9/10	8/9	5/5	9/10	8/9	10/10	5/5	7/10	19/20
Hemorrhage	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–
Brown Pigment	–	1/9	2/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/9	–	–	–	–	–	–	–
Granuloma	–	1/9	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 1

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control
MANDIBULAR LYMPH NODE (contd)																										
Edema/Lymphostasis	3/10	3/9	4/10	5/10	4/10	3/9	5/10	2/5	7/10	5/9	6/9	–	3/10	5/9	4/9	2/5	2/10	4/10	4/9	2/5	8/10	4/9	3/10	3/5	2/10	6/20
Congestion	–	–	–	–	1/10	–	–	–	–	–	–	–	–	2/9	1/9	–	–	1/10	–	–	–	1/9	–	–	–	–
Particles	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–
MANDIBULAR SALIVARY GLAND																										
Mononuclear Cell Infiltrate	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2/9	–	–	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20
SUBCUTANEOUS LYMPH NODES																										
Hyperplasia	–	–	–	1/1	–	–	1/1	–	–	–	1/1	1/1	–	–	–	–	–	–	1/1	1/1	–	–	–	1/1	1/1	3/3
Lymphostasis/Edema	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–
SKIN																										
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–
ADIPOSE TISSUE																										
Particles	-	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 1

ORGAN Lesion	Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control
CONNECTIVE TISSUE																											
Particles		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	–	–	–
Inflammation		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	–	–	–	–

E.4 Histopathology Summary Table, Second Replicate

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion	Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control	Gelatin Saline
LUNGS																												
Particles		10/10	10/10	10/10	3/10	10/10	10/10	10/10	5/10	10/10	10/10	10/10	5/5	10/10	10/10	10/10	5/5	10/10	10/10	10/10	5/5	10/10	10/10	10/10	5/5	10/10	—	—
Inflammatory Reaction		10/10	7/10	8/10	—	10/10	10/10	10/10	5/10	9/10	7/10	6/10	5/5	10/10	10/10	9/10	3/5	9/10	3/10	3/10	5/5	6/10	6/10	5/10	5/5	8/10	—	—
Granuloma		10/10	4/10	2/10	—	10/10	5/10	5/10	1/10	7/10	7/10	6/10	1/5	10/10	10/10	10/10	1/5	2/10	1/10	—	—	2/10	4/10	2/10	—	3/10	—	—
Fibrosis		5/10	1/10	1/10	—	6/10	3/10	4/10	—	2/10	—	—	—	6/10	3/10	—	—	—	1/10	—	—	—	1/10	—	—	3/10	—	—
Hyperplasia, Adenomatous		10/10	9/10	7/10	3/10	10/10	9/10	7/10	3/10	3/10	7/10	4/10	2/5	8/10	8/10	5/10	3/5	9/10	3/10	5/10	4/5	6/10	6/10	2/10	4/5	8/10	2/20	4/10
Hyperplasia, Papillary		1/10	1/10	—	—	5/10	—	—	—	1/10	—	—	—	5/10	—	—	1/5	2/10	—	—	—	—	2/10	—	—	1/10	—	—
Metaplasia, Ciliary		4/10	—	1/10	—	7/10	3/10	—	—	2/10	2/10	—	—	8/10	6/10	—	2/5	5/10	—	1/10	—	1/10	2/10	1/10	2/5	3/10	—	—
Metaplasia, Squamous		—	—	—	—	—	1/10	—	—	—	—	—	—	5/10	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Adenoma		—	1/10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Mononuclear Cell Infiltrate		7/10	8/10	7/10	5/10	6/10	8/10	7/10	4/10	7/10	6/10	8/10	4/5	8/10	8/10	6/10	—	6/10	2/10	2/10	3/5	3/10	3/10	4/10	1/5	6/10	8/20	4/10
Congestion		6/10	3/10	4/10	2/10	8/10	6/10	7/10	5/10	2/10	3/10	7/10	2/5	9/10	8/10	7/10	4/5	6/10	4/10	3/10	3/5	8/10	8/10	5/10	2/5	8/10	7/20	3/10
Hemorrhage		—	2/10	2/10	—	1/10	1/10	—	—	3/10	2/10	—	2/5	1/10	—	1/10	1/5	—	1/10	—	—	1/10	3/10	1/10	2/5	1/10	—	—
Pneumonia		—	2/10	—	—	2/10	—	—	1/10	1/10	2/10	3/10	2/5	1/10	3/10	3/10	1/5	2/10	1/10	2/10	4/5	1/10	2/10	2/10	1/5	—	—	2/10
Emphysema		5/10	2/10	—	—	9/10	5/10	—	2/10	3/10	2/10	4/10	1/5	9/10	4/10	3/10	1/5	3/10	2/10	2/10	4/5	2/10	4/10	4/10	3/5	4/10	—	2/10
Foreign Body		1/10	1/10	3/10	2/10	3/10	1/10	—	1/10	1/10	1/10	3/10	1/5	2/10	—	1/10	1/5	—	2/10	—	—	1/10	2/10	2/10	—	—	2/20	2/10
Proliferation, Fibroblastic		1/10	—	—	—	2/10	1/10	—	—	—	—	—	—	—	—	—	—	—	1/10	—	—	—	—	—	—	3/10	—	—

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
TRACHEA																											
Particles	8/10	10/10	8/10	–	10/10	10/10	10/10	4/10	6/10	7/10	2/10	3/5	10/10	5/10	9/10	4/5	6/10	6/10	3/10	4/5	9/10	7/10	3/10	5/5	8/10	–	–
Inflammatory Reaction	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	1/10	1/5	1/10	1/10	–	–	3/10	–	–
Hyperplasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2/10	–	–
Mineralization	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Polyp	–	–	–	–	3/10	–	–	–	1/10	–	–	1/5	1/10	–	1/10	–	–	–	–	–	–	1/10	–	–	–	–	–
Submucosal Gland-Ectasia	–	–	–	–	2/10	1/10	–	1/10	1/10	1/10	2/10	1/5	4/10	1/10	2/10	1/5	2/10	1/10	–	2/5	2/10	3/10	4/10	1/5	1/10	2/20	–
Submucosal Gland-Atrophy	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Papillomatosis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	3/10	–	–
Squamous Cell Carcinoma	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–
THYROIDS																											
Ectasia	8/10	7/10	6/10	10/10	9/10	7/10	8/10	3/10	6/10	7/10	9/10	4/5	7/10	6/10	5/10	4/5	8/10	8/10	6/10	4/5	7/10	9/10	9/10	3/5	10/10	18/20	9/10
Cysts	3/10	5/10	1/10	3/10	–	2/10	3/10	1/10	1/10	2/10	3/10	1/5	1/10	3/10	3/10	–	2/10	5/10	2/10	2/5	7/10	5/10	4/10	1/5	3/10	9/20	3/10
Proliferation	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Amyloidosis	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Hyperplasia	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Atrophy	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–
Adenoma	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Carcinoma	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	1/10	–	–

HISTOPATHOLOGY SUMMARY TABLE

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Male Syrian Hamsters
Replicate 2

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
PLEURA																											
Particles	5/10	–	–	–	6/10	4/10	1/10	–	2/10	–	1/10	–	4/10	3/10	–	–	–	–	–	–	–	2/10	–	–	2/10	–	–
Inflammatory Reaction	4/10	1/10	2/10	–	9/10	8/10	2/10	–	2/10	1/10	1/10	2/5	8/10	5/10	–	–	4/10	–	–	–	1/10	3/10	1/10	1/5	1/10	–	–
Fibrosis	7/10	3/10	–	–	5/10	1/10	1/10	–	2/10	–	–	–	4/10	3/10	–	1/5	–	–	–	–	–	2/10	1/10	–	5/10	–	–
Proliferation, Fibroblastic	1/10	–	–	–	3/10	1/10	1/10	1/10	3/10	–	2/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mesothelioma	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mononuclear Cell Infiltrate	–	–	–	–	1/10	–	–	–	–	–	1/10	–	–	–	1/10	–	–	–	–	–	–	–	–	–	1/10	–	–
Edema	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
LARYNX																											
Particles	4/10	1/10	3/10	–	6/10	1/10	4/10	–	–	–	1/10	–	1/10	–	1/10	2/5	–	–	–	–	2/10	2/10	1/10	–	5/10	–	–
Inflammatory Reaction	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	1/10	–	–	1/10	–	–
Mononuclear Cell Infiltrate	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–
Submucosal Gland-Proliferation	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Submucosal Gland-Ectasia	–	–	–	–	–	–	–	1/10	–	1/10	–	1/5	2/10	2/10	1/10	–	–	3/10	–	1/5	1/10	–	1/10	1/5	–	2/20	–
Submucosal Gland-Abscess	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Submucosal Gland-Cysts	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20	–
Hyperplasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion	Group: DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
THYROIDS (contd)																											
Papillary Fibrocystoma	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–
PARATHYROIDS																											
Hyperplasia	–	–	1/10	–	–	2/10	1/10	–	3/10	–	4/10	1/5	2/10	1/10	–	–	–	1/10	–	–	3/10	–	1/10	–	1/10	–	–
Adenoma	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	1/5	–	–	–	–	–	1/20	–
Cyst	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	1/10	–	–	–	–	–	–	–	–	1/10
ESOPHAGUS	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
BRAIN																											
Congestion	8/10	7/10	6/10	6/10	9/10	6/10	5/10	3/10	6/10	8/10	9/10	4/5	6/10	4/10	4/10	2/5	10/10	5/10	2/10	4/5	5/10	6/10	6/10	1/5	8/10	7/20	5/10
Edema	7/10	4/10	5/10	6/10	5/10	6/10	5/10	1/10	5/10	4/10	4/10	1/5	1/10	3/10	3/10	1/5	3/10	5/10	3/10	–	4/10	7/10	5/10	1/5	5/10	11/20	5/10
Hemorrhage	–	–	–	–	–	–	–	–	–	–	1/10	–	–	1/10	–	–	–	–	–	–	–	1/10	2/10	–	1/10	–	–
Mononuclear Cell Infiltrate	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–
SPINAL CORD																											
Congestion	–	1/10	–	1/10	–	1/10	–	1/10	–	–	2/10	1/5	–	–	–	–	–	–	–	–	–	–	–	–	4/10	1/20	–
Hemorrhage	–	–	–	–	–	1/10	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

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Male Syrian Hamsters
Replicate 2

HISTOPATHOLOGY SUMMARY TABLE

ORGAN Lesion	Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
EYES																												
Cataract		–	1/10	–	–	–	–	–	–	–	–	1/10	–	–	–	1/10	–	1/10	–	–	1/5	–	–	1/10	–	–	–	–
Retroocular Tissue-Mineralization		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20	–
PITUITARY																												
Vacuolization		8/10	10/10	9/10	10/10	10/10	8/10	10/10	5/10	9/10	9/10	9/10	5/5	9/10	9/10	9/10	4/5	10/10	9/10	10/10	5/5	10/10	10/10	10/10	5/5	10/10	20/20	9/10
Congestion		2/10	4/10	2/10	1/10	3/10	2/10	3/10	1/10	1/10	4/10	5/10	3/5	–	3/10	1/10	–	–	–	–	–	2/10	4/10	4/10	–	6/10	4/20	1/10
Cyst		1/10	1/10	–	1/10	–	–	–	–	–	–	–	2/5	1/10	–	1/10	–	2/10	2/10	1/10	–	–	2/10	3/10	1/5	1/10	2/20	–
Amyloidosis		–	1/10	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
ADRENAL CORTEX																												
Hyperplasia		2/10	5/10	3/10	7/10	2/10	2/10	3/10	3/10	3/10	3/10	7/10	3/5	5/10	5/10	4/10	1/5	4/10	5/10	3/10	3/5	4/10	2/10	3/10	2/5	5/10	6/20	2/10
Adenoma		–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10
Brown Pigment		3/10	–	1/10	–	2/10	4/10	2/10	1/10	–	2/10	1/10	1/5	4/10	5/10	3/10	2/5	4/10	5/10	–	1/5	5/10	5/10	3/10	2/5	2/10	4/20	–
Amyloidosis		1/10	–	–	2/10	2/10	1/10	–	–	–	–	–	–	3/10	–	2/10	–	–	–	–	–	–	–	1/10	–	–	–	–
Hemorrhage		–	–	–	–	–	–	–	–	–	–	–	–	2/10	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–
Congestion		–	–	–	–	–	–	–	–	–	–	–	–	2/10	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10
Vacuolization		5/10	2/10	3/10	6/10	–	–	1/10	–	8/10	4/10	4/10	3/5	1/10	2/10	1/10	–	4/10	2/10	1/10	2/5	1/10	2/10	1/10	1/5	4/10	13/20	3/10
Degeneration, Vacuolar		–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control	Gelatin Saline
ADRENAL CORTEX (contd)																											
Cyst	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1/10	-	-	-	-	-
Atrophy	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1/10
ADRENAL MEDULLA																											
Congestion	-	-	-	-	-	-	-	-	-	1/10	-	-	3/10	-	1/10	-	-	-	-	-	-	-	-	-	-	-	-
Mononuclear Cell Infiltrate	-	-	-	-	-	-	1/10	-	-	-	-	-	1/10	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Brown Pigment	-	-	-	-	-	-	-	-	-	1/10	-	-	1/10	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Pheochromocytoma	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1/10
SPLEEN																											
Brown Pigment	-	-	-	-	-	-	-	-	-	-	-	-	2/10	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Fibrosis	-	-	-	-	-	-	-	-	-	-	-	-	-	1/10	-	-	-	-	-	-	-	-	-	-	-	-	-
Amyloidosis	-	-	-	2/10	1/10	1/10	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1/10	-	-	-	-
Congestion	-	-	-	-	-	-	-	-	-	-	-	-	1/10	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Perisplenitis	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1/10	-	-	-	-	-	-	-	-	-	1/10	-	-
Membrane-Inflammatory Cell	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	1/10	-	-	-	-

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
PANCREAS																											
Cysts	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–
Fatty Infiltration	–	–	1/10	1/10	–	–	–	1/10	1/10	–	–	–	1/10	–	–	–	–	–	1/10	–	–	1/10	–	1/5	1/10	1/20	–
Adenoma	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Duct-Ectasia	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–
HEART																											
Congestion	4/10	4/10	6/10	3/10	6/10	4/10	7/10	3/10	4/10	4/10	8/10	3/5	6/10	2/10	4/10	2/5	4/10	4/10	1/10	2/5	2/10	6/10	6/10	1/5	9/10	9/20	3/10
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Hemorrhage	–	1/10	–	–	2/10	–	1/10	2/10	1/10	–	–	–	–	–	2/10	–	–	–	–	–	1/10	2/10	3/10	–	2/10	3/20	1/10
Particles	–	1/10	2/10	–	1/10	1/10	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Fibrosis	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Mononuclear Cell Infiltrate	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10
Sclerosis	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Brown Pigment	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Arteritis	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE$_2$O$_3$ - 5 mg	DP: FE$_2$O$_3$ - 2.5 mg	DP: FE$_2$O$_3$ - 1.25 mg	DP: FE$_2$O$_3$ - Solvent	DE: FE$_2$O$_3$ - 5 mg	DE: FE$_2$O$_3$ - 2.5 mg	DE: FE$_2$O$_3$ - 1.25 mg	DE: FE$_2$O$_3$ - Solvent	COE: FE$_2$O$_3$ - 5 mg	COE: FE$_2$O$_3$ - 2.5 mg	COE: FE$_2$O$_3$ - 1.25 mg	COE: FE$_2$O$_3$ - Solvent	CSC: FE$_2$O$_3$ - 5 mg	CSC: FE$_2$O$_3$ - 2.5 mg	CSC: FE$_2$O$_3$ - 1.25 mg	CSC: FE$_2$O$_3$ - Solvent	RTE: FE$_2$O$_3$ - 5 mg	RTE: FE$_2$O$_3$ - 2.5 mg	RTE: FE$_2$O$_3$ - 1.25 mg	RTE: FE$_2$O$_3$ - Solvent	BP: FE$_2$O$_3$ - 2 mg	Colony Control	Gelatin Saline
KIDNEYS																											
Nephropathy	10/10	10/10	10/10	9/10	10/10	10/10	10/10	5/10	10/10	9/10	10/10	5/5	9/10	10/10	10/10	5/5	10/10	10/10	10/10	5/5	10/10	10/10	9/10	5/5	10/10	20/20	10/10
Nephrosclerosis	1/10	5/10	1/10	3/10	3/10	4/10	4/10	–	1/10	2/10	3/10	1/5	3/10	7/10	3/10	2/5	3/10	7/10	2/10	3/5	7/10	6/10	5/10	2/5	3/10	10/20	–
Amyloidosis	–	–	–	2/10	1/10	–	–	–	–	–	–	–	2/10	–	1/10	–	–	–	–	–	–	–	1/10	–	–	–	–
Mineralization	4/10	7/10	7/10	4/10	5/10	7/10	8/10	4/10	7/10	9/10	9/10	3/5	9/10	8/10	8/10	5/5	10/10	9/10	10/10	5/5	10/10	10/10	8/10	5/5	10/10	17/20	8/10
Congestion	2/10	4/10	1/10	2/10	1/10	1/10	3/10	1/10	–	7/10	1/10	2/5	–	–	–	–	1/10	–	–	–	2/10	2/10	3/10	1/5	3/10	4/20	3/10
Hemorrhage	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Nephritis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–
Proliferation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20	–
LIVER																											
Congestion	7/10	7/10	8/10	5/10	8/10	6/10	6/10	5/10	6/10	6/10	8/10	4/5	6/10	9/10	7/10	3/5	8/10	8/10	6/10	5/5	8/10	9/10	9/10	4/5	8/10	14/20	5/10
Hemorrhage	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	1/20	–
Degeneration, Vacuolar	4/10	7/10	6/10	9/10	6/10	8/10	8/10	4/10	7/10	5/10	6/10	4/5	2/10	5/10	5/10	3/5	7/10	9/10	7/10	2/5	8/10	9/10	3/10	2/5	9/10	10/20	9/10
Degeneration, Granular	5/10	5/10	9/10	3/10	8/10	9/10	9/10	5/10	10/10	8/10	10/10	5/5	10/10	10/10	8/10	5/5	10/10	9/10	9/10	5/5	9/10	7/10	8/10	5/5	9/10	8/20	8/10
Amyloidosis	1/10	–	–	2/10	2/10	1/10	–	–	–	–	–	–	3/10	–	1/10	–	–	1/10	–	–	–	–	1/10	–	–	–	–
Brown Pigment	1/10	–	–	2/10	2/10	1/10	1/10	–	–	1/10	1/10	–	4/10	1/10	2/10	–	2/10	2/10	–	–	1/10	4/10	1/10	–	1/10	1/20	2/10
Extramedullary Hematopoiesis	–	1/10	1/10	2/10	–	2/10	–	–	3/10	1/10	–	–	–	–	1/10	–	–	–	1/10	–	2/10	1/10	1/10	1/5	–	5/20	–
Proliferation, Bile Duct	–	–	–	–	1/10	1/10	1/10	–	–	–	–	1/5	1/10	–	1/10	–	–	–	–	–	–	–	1/10	–	–	–	–
Mononuclear Cell Infiltrate	–	–	–	–	–	1/10	–	–	–	1/10	–	–	–	–	–	–	1/10	1/10	1/10	–	–	1/10	–	1/5	–	–	–

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Male Syrian Hamsters
Replicate 2

HISTOPATHOLOGY SUMMARY TABLE

ORGAN Lesion	Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
LIVER (contd)																												
Dilatation, Bile Duct		—	—	—	—	—	—	1/10	—	—	—	1/10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Inflammatory Cell		4/10	8/10	7/10	9/10	8/10	6/10	7/10	3/10	6/10	9/10	10/10	4/5	7/10	6/10	7/10	2/5	10/10	9/10	6/10	3/5	9/10	9/10	9/10	3/5	8/10	12/20	9/10
Granuloma		—	—	—	—	—	1/10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1/10	—	—	—	—	—	—
Particles		—	—	1/10	—	3/10	1/10	—	1/10	—	—	1/10	—	—	1/10	1/10	—	1/10	—	—	—	—	—	—	—	—	—	—
Disassociation, Hepatocellular		—	—	—	—	—	—	1/10	—	—	—	1/10	1/5	1/10	—	—	—	1/10	1/10	—	—	—	—	2/10	—	—	—	—
Cyst		—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1/10	—	—	—	—	—	—	—	—	—	—
Hemangioma		—	—	—	—	—	1/10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Necrosis		—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1/20	—
GALL BLADDER																												
Stone		—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1/10	—	—	—	1/10	—	—	—	—	—	—
Ectasia		—	—	—	—	—	—	1/10	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Mononuclear Cell Infiltrate		—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1/10	—	—	—	—	—	—	—	—
Atrophy		—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1/20	—
Inflammation		—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	1/5	—	—	—

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
TESTES																											
Atrophy	–	2/10	–	–	–	–	1/10	1/10	–	3/10	–	–	–	–	1/10	–	2/10	2/10	–	1/5	–	–	–	–	–	2/20	–
Hypospermia	–	4/10	1/10	1/10	1/10	1/10	1/10	1/10	–	1/10	–	1/5	–	–	1/10	1/5	2/10	2/10	–	–	–	2/10	1/10	–	–	1/20	–
Hypoplasia	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Hyperspermia	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–
Hyperplasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–
SEMINAL VESICLES																											
Mineralization	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2/2	–	1/1	–	–	–	–	1/1	2/2	–
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	–	–	–	1/1	–	1/1	–	–
URINARY BLADDER																											
Hyperplasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	2/10	–	–	–	1/20	–
Edema	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	1/10	1/10	–	–	–	–	1/5	–	–	–	–	–	–	–	–	–	–	–
Papilloma	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20	–
Squamous Metaplasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
PROSTATE																											
Hyperplasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–
Hyperplasia, Adenomatous	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
THYMUS																											
Cyst(s)	–	–	–	–	3/10	1/10	1/10	1/10	4/10	1/10	–	–	–	–	4/10	1/5	1/10	–	1/10	–	–	–	2/10	–	–	4/20	1/10
Hyperplasia (Epithelial)	1/10	2/10	3/10	4/10	5/10	2/10	2/10	1/10	2/10	2/10	2/10	2/5	1/10	1/10	1/10	2/5	4/10	2/10	2/10	–	1/10	1/10	3/10	2/5	2/10	3/20	3/10
Particles	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
THORACIC LYMPH NODES																											
Particles	10/10	10/10	10/10	2/10	10/10	10/10	10/10	5/10	9/10	9/10	6/10	5/5	10/10	10/10	10/10	5/5	9/10	9/10	6/10	5/5	10/10	10/10	9/10	5/5	9/10	–	–
Hyperplasia	5/10	2/10	2/10	2/10	5/10	4/10	1/10	2/10	6/10	4/10	2/10	–	1/10	2/10	1/10	–	2/10	2/10	1/10	1/5	–	–	–	–	–	–	–
Lymphostasis/Edema	–	–	1/10	–	1/10	–	1/10	–	–	–	–	–	1/10	–	1/10	–	1/10	2/10	2/10	2/5	–	1/10	–	4/5	1/10	–	–
Hemorrhage	2/10	1/10	1/10	–	–	1/10	1/10	2/10	–	1/10	1/10	–	1/10	–	2/10	1/5	2/10	2/10	–	–	–	2/10	–	–	1/10	2/20	3/10
Congestion	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20	–
Brown Pigment	2/10	1/10	2/10	1/10	1/10	–	–	1/10	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	3/20	5/10
Granuloma	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	9/10	–	–
NASAL TURBINATES	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

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Male Syrian Hamsters
Replicate 2

ORGAN Lesion / Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
STERNUM (BONE MARROW)	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
SMALL INTESTINE																											
Inflammation	1/10	1/10	–	2/10	1/10	3/10	2/10	–	1/10	1/10	4/10	2/5	1/10	1/10	1/10	1/5	2/10	1/10	1/10	1/5	2/10	–	3/10	1/5	3/10	2/20	1/10
Parasite	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
LARGE INTESTINE																											
Inflammation	–	2/10	1/10	4/10	4/10	2/10	2/10	–	1/10	1/10	4/10	–	3/10	1/10	3/10	–	1/10	2/10	2/10	1/5	2/10	1/10	1/10	1/5	4/10	3/20	2/10
Parasite	–	–	1/10	–	–	–	–	–	–	1/10	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–
Abscess	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
STOMACH																											
Hyperplasia	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–
Mineralization	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	1/10	–	–
Proliferation	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Inflammation	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–
MANDIBULAR LYMPH NODE																											
Hyperplasia	9/10	7/10	7/10	7/10	7/10	7/10	6/10	5/10	9/10	4/10	6/10	2/5	7/10	8/10	8/10	4/5	9/10	5/10	6/10	1/5	8/10	9/10	4/10	3/5	7/10	15/20	7/10
Hemorrhage	–	–	–	1/10	–	1/10	–	–	–	1/10	1/10	1/5	–	–	–	–	1/10	–	–	–	–	–	–	–	–	1/20	2/10

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
MANDIBULAR LYMPH NODE (contd)																											
Brown Pigment	2/10	–	–	1/10	–	–	1/10	1/10	–	–	–	–	1/10	–	–	1/5	1/10	–	–	–	–	1/10	–	–	–	2/20	2/10
Edema/Lymphostasis	6/10	9/10	9/10	5/10	5/10	5/10	6/10	1/10	4/10	6/10	6/10	3/5	6/10	6/10	6/10	3/5	5/10	7/10	8/10	5/5	8/10	6/10	7/10	4/5	7/10	11/20	6/10
Congestion	–	–	–	2/10	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	1/20	–
Lymphoma	–	–	–	–	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Fibrosis	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/5	–	–	–	–	–	–	–	–	–	–	–
MANDIBULAR SALIVARY GLAND																											
Mononuclear Cell Infiltrate	–	1/10	1/10	1/10	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	2/10	–	–	–	1/10	–	–	1/20	2/10
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/20	–
Mixed Tumor	–	–	–	–	–	–	–	–	1/10	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
SUBCUTANEOUS LYMPH NODES																											
Hyperplasia	–	–	–	–	1/1	–	–	1/1	–	–	1/1	–	–	–	–	–	–	–	–	–	–	–	1/1	1/1	–	1/1	2/2
Lymphostasis/Edema	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	1/1
Congestion	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
SKIN																											
Inflammation	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–
Sebaceous Gland-Hyperplasia	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–

HISTOPATHOLOGY SUMMARY TABLE

L6119/6138
Male Syrian Hamsters
Replicate 2

ORGAN Lesion	Group	DP - 5 mg	DP - 2.5 mg	DP - 1.25 mg	DP - Solvent	DP: FE_2O_3 - 5 mg	DP: FE_2O_3 - 2.5 mg	DP: FE_2O_3 - 1.25 mg	DP: FE_2O_3 - Solvent	DE: FE_2O_3 - 5 mg	DE: FE_2O_3 - 2.5 mg	DE: FE_2O_3 - 1.25 mg	DE: FE_2O_3 - Solvent	COE: FE_2O_3 - 5 mg	COE: FE_2O_3 - 2.5 mg	COE: FE_2O_3 - 1.25 mg	COE: FE_2O_3 - Solvent	CSC: FE_2O_3 - 5 mg	CSC: FE_2O_3 - 2.5 mg	CSC: FE_2O_3 - 1.25 mg	CSC: FE_2O_3 - Solvent	RTE: FE_2O_3 - 5 mg	RTE: FE_2O_3 - 2.5 mg	RTE: FE_2O_3 - 1.25 mg	RTE: FE_2O_3 - Solvent	BP: FE_2O_3 - 2 mg	Colony Control	Gelatin Saline
ADIPOSE TISSUE																											
Particles		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–
Inflammation		–	–	–	–	1/1	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	–	–	–	1/1	–
CONNECTIVE TISSUE																											
Particles		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	1/1	–	–
MESENTERIC LYMPH NODE																											
Hyperplasia		–	–	–	–	1/1	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	1/1	–	–	–	–	1/1	–
Lymphostasis		–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	–	–	–	–	–	–	–
Brown Pigment		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–
PERITONEUM																											
Inflammation		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–	–	–	–	–	–	–	–	–	–
THORACIC CAVITY																											
Cyst		–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	–	1/1	–

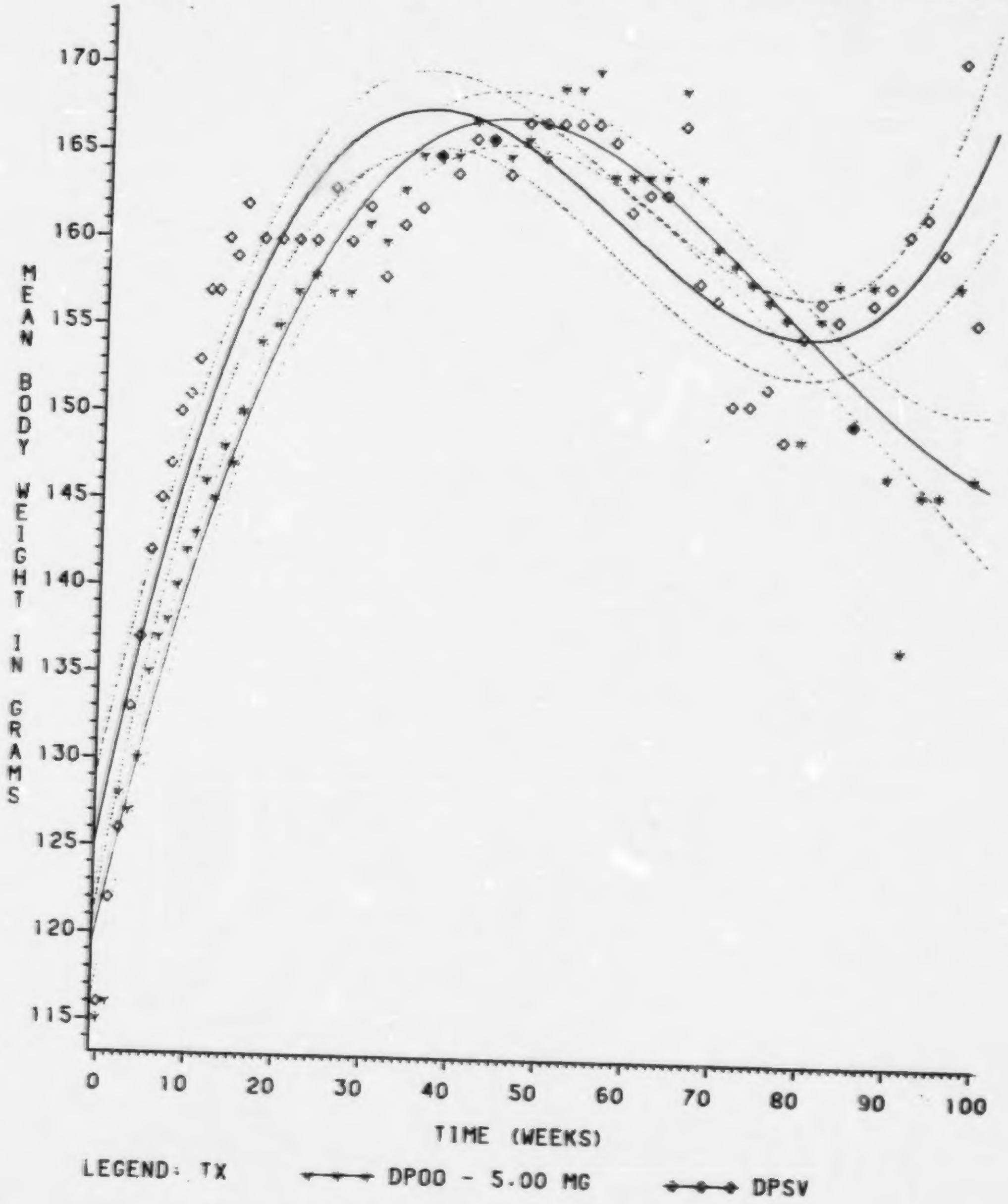
APPENDIX F

COMPUTER GENERATED BODY WEIGHT CURVES

F.1 First Replicate

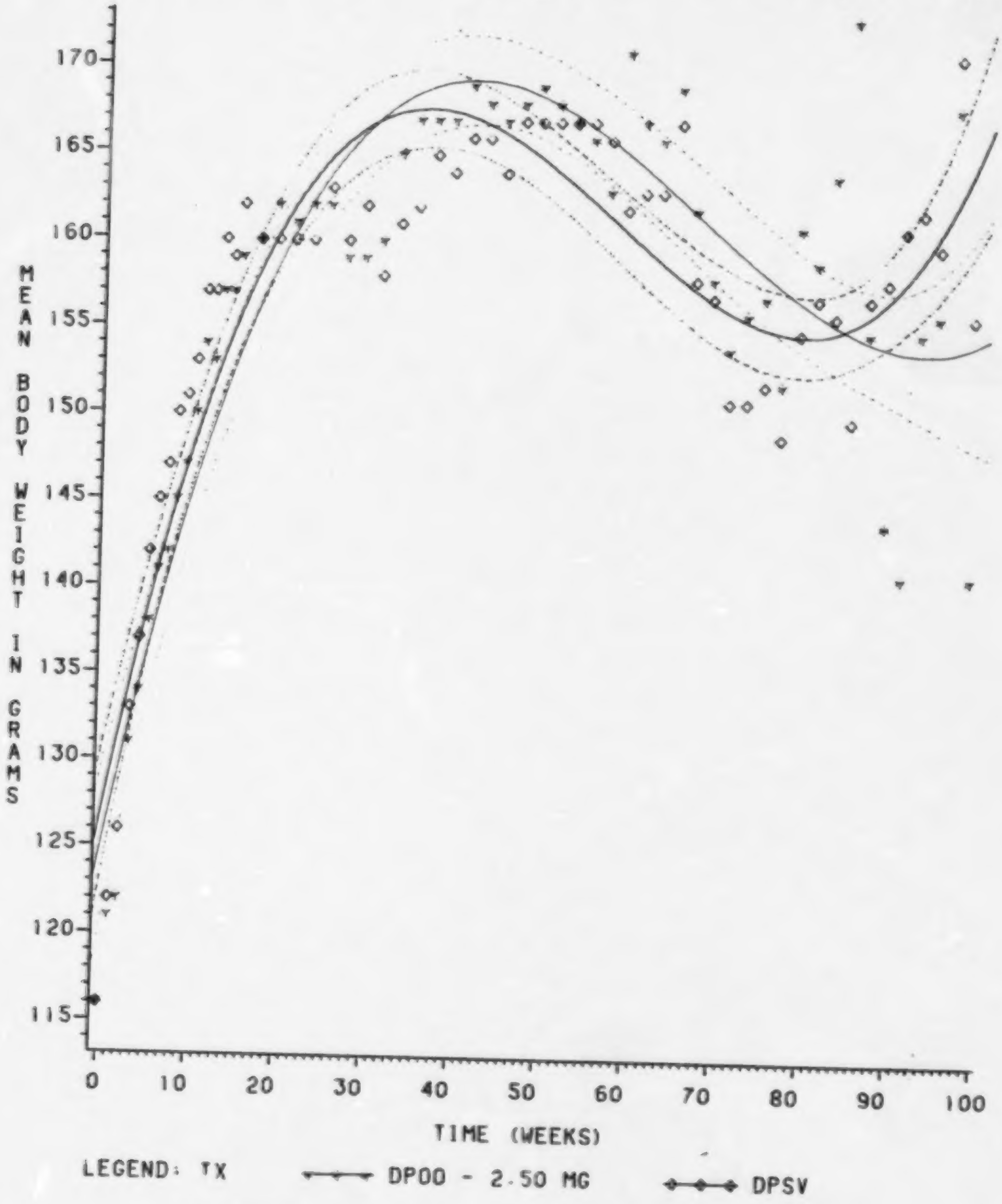
COMPOUND DPOO(HIGH DOSE) AND DPSV

MEAN BODY WEIGHT VS TIME – REPLICATION 1



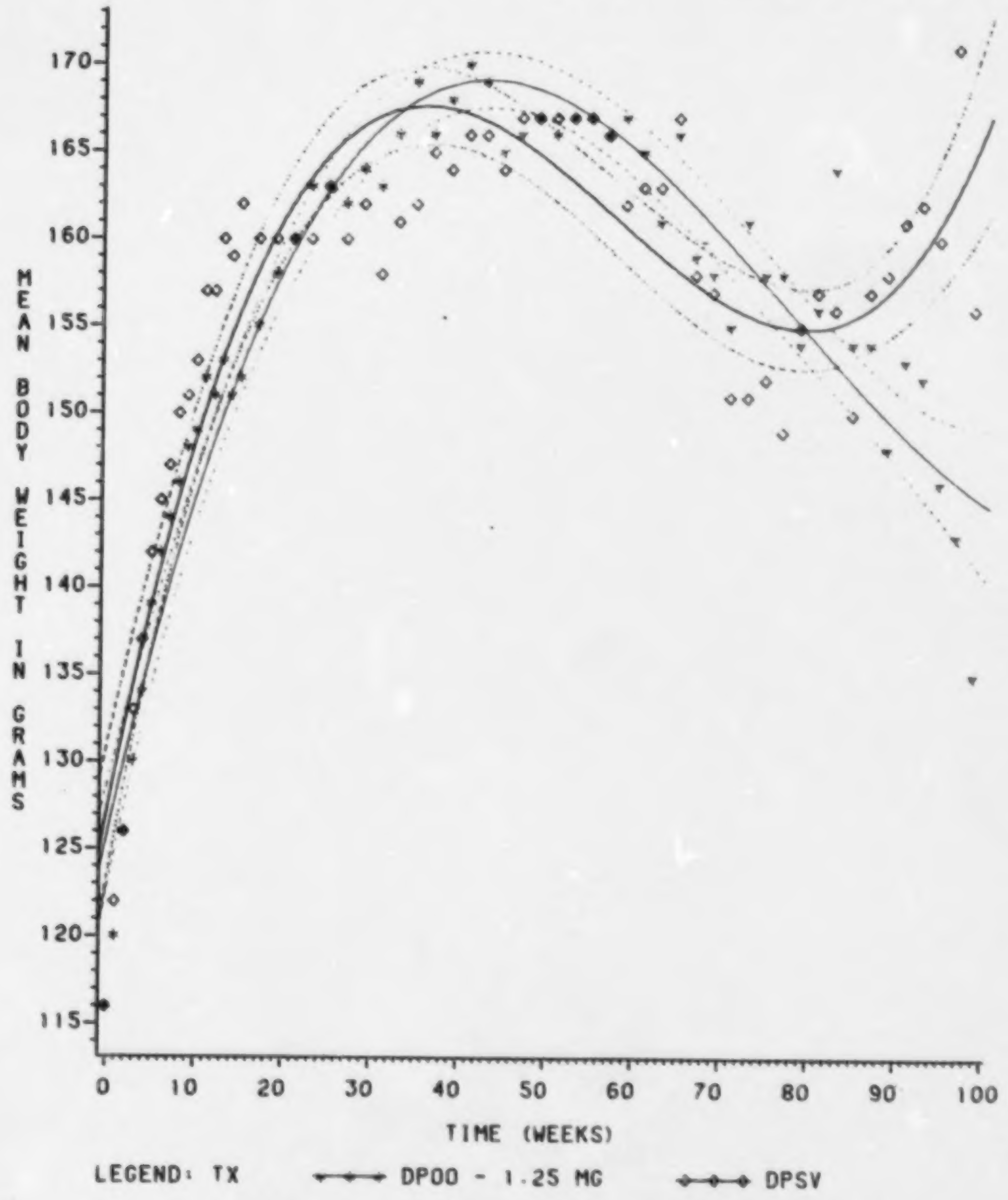
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DPOO(MEDIUM DOSE) AND DPSV
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

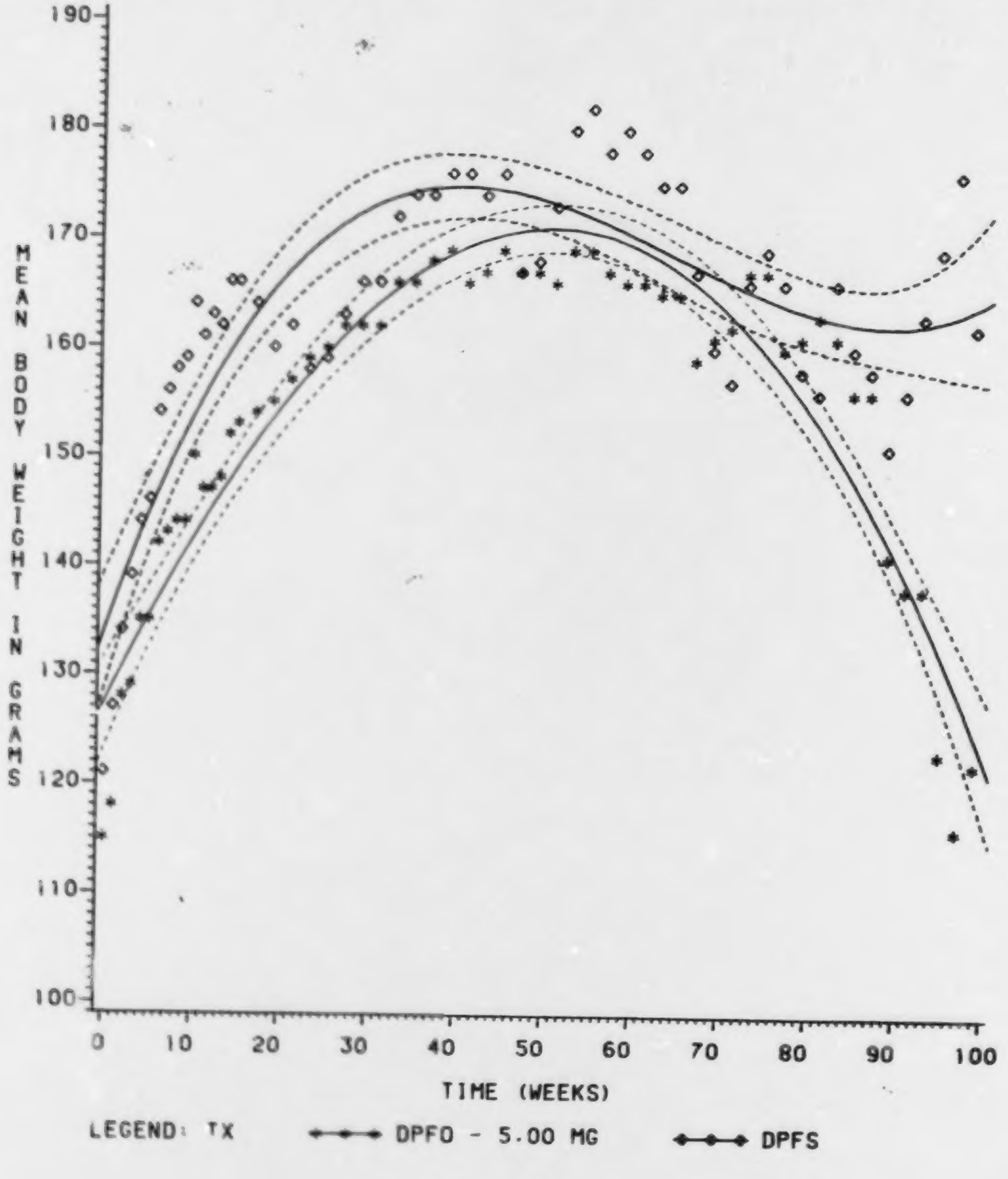
COMPOUND DPOO(LOW DOSE) AND DPSV
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

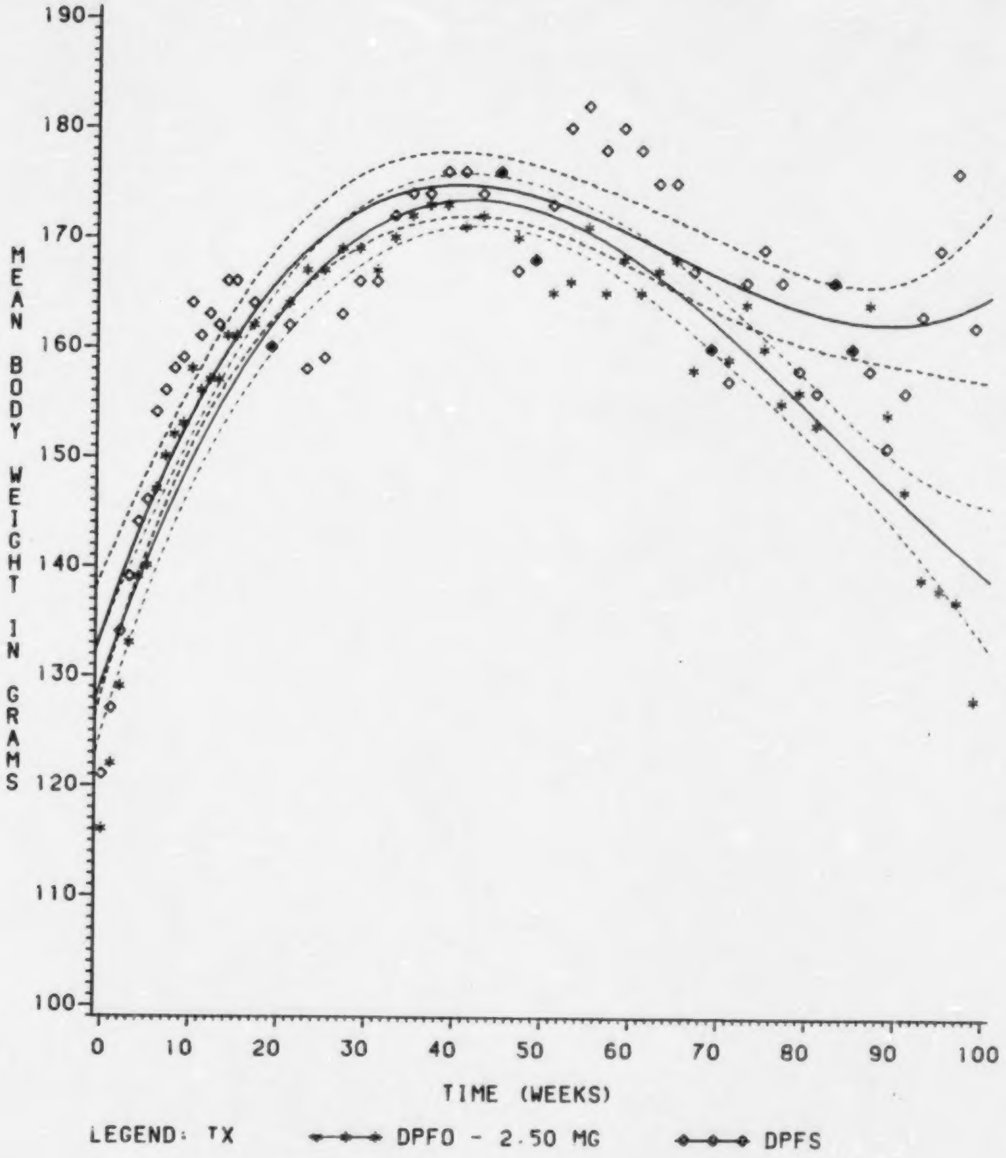
COMPOUND DPFO(HIGH DOSE) AND DPFS

MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

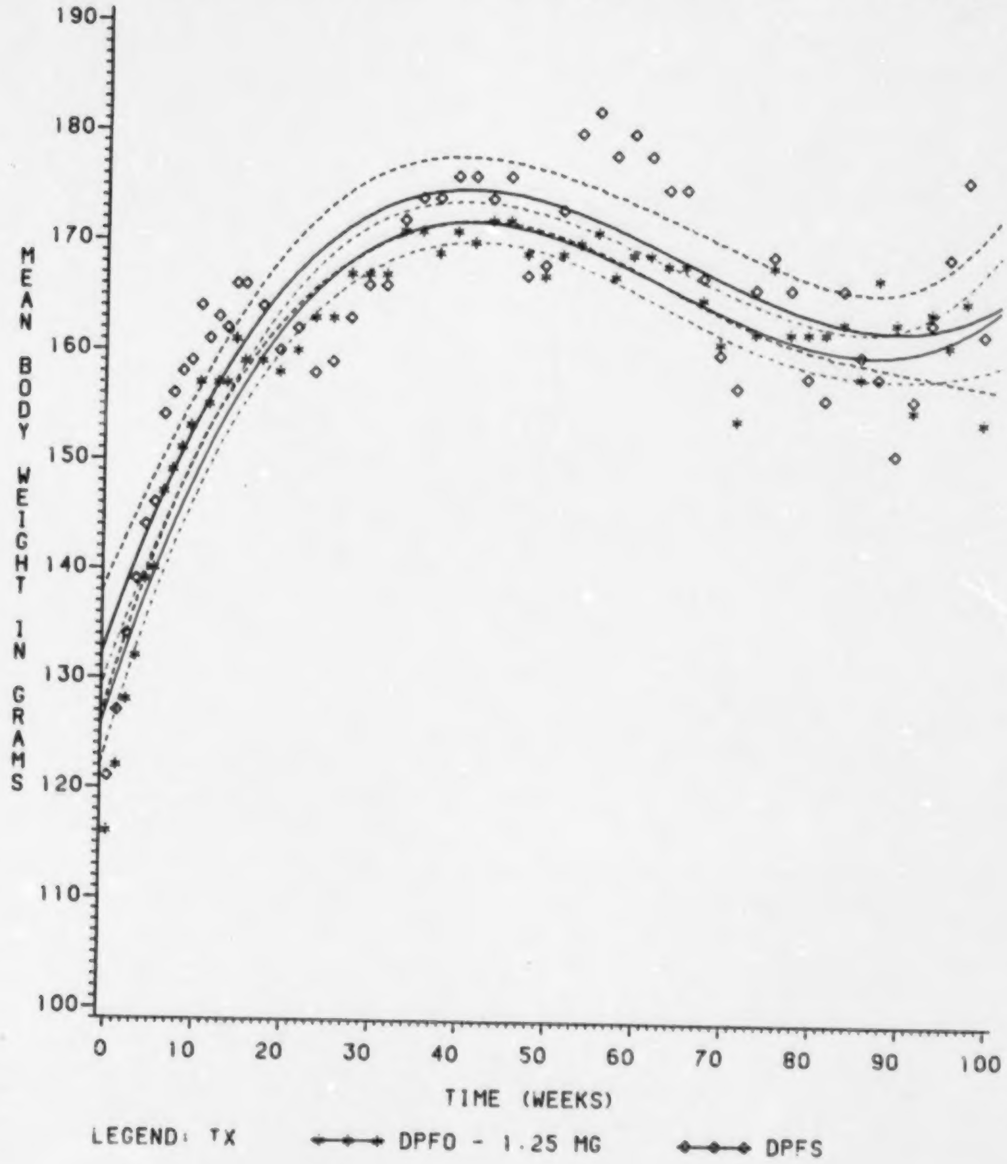
COMPOUND DPFO(MEDIUM DOSE) AND DPFS
MEAN BODY WEIGHT VS TIME - REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DPFO(LOW DOSE) AND DPFS

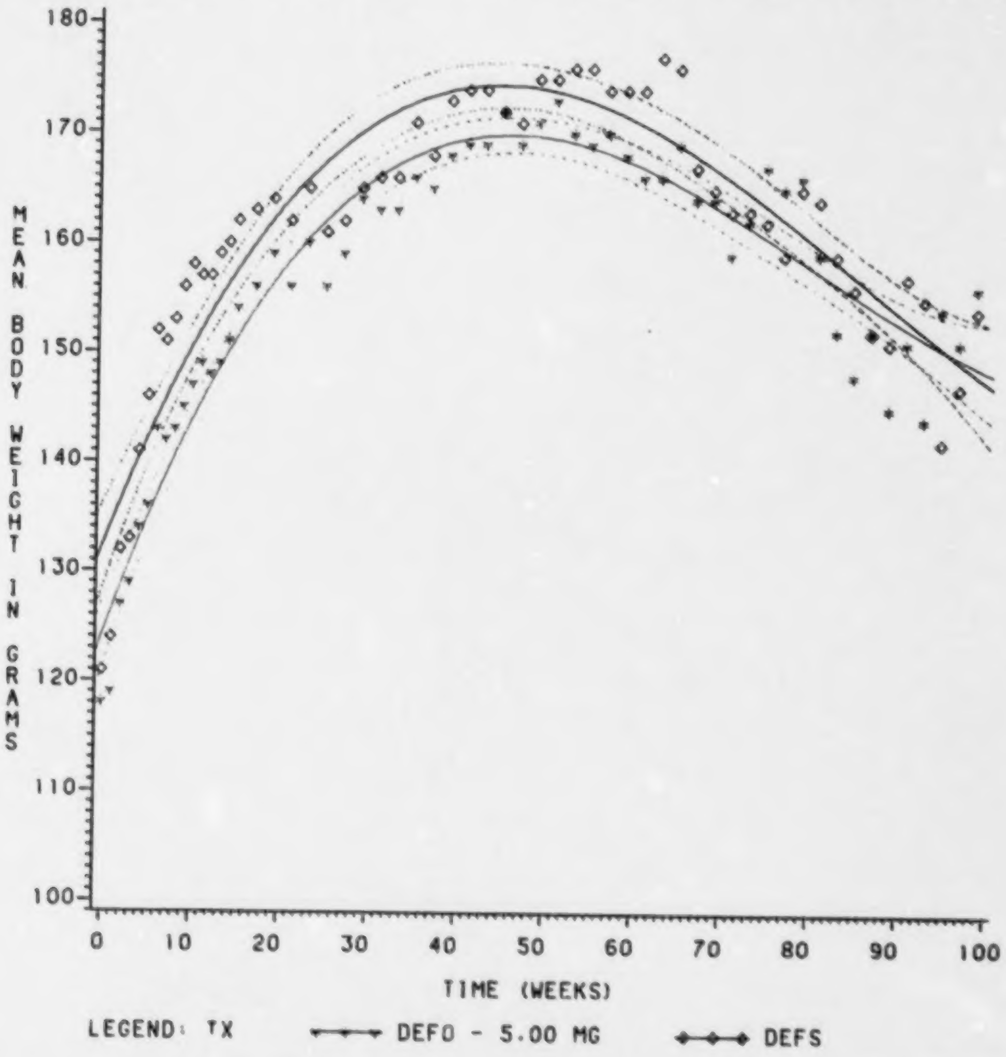
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DEFO(HIGH DOSE) AND DEFS

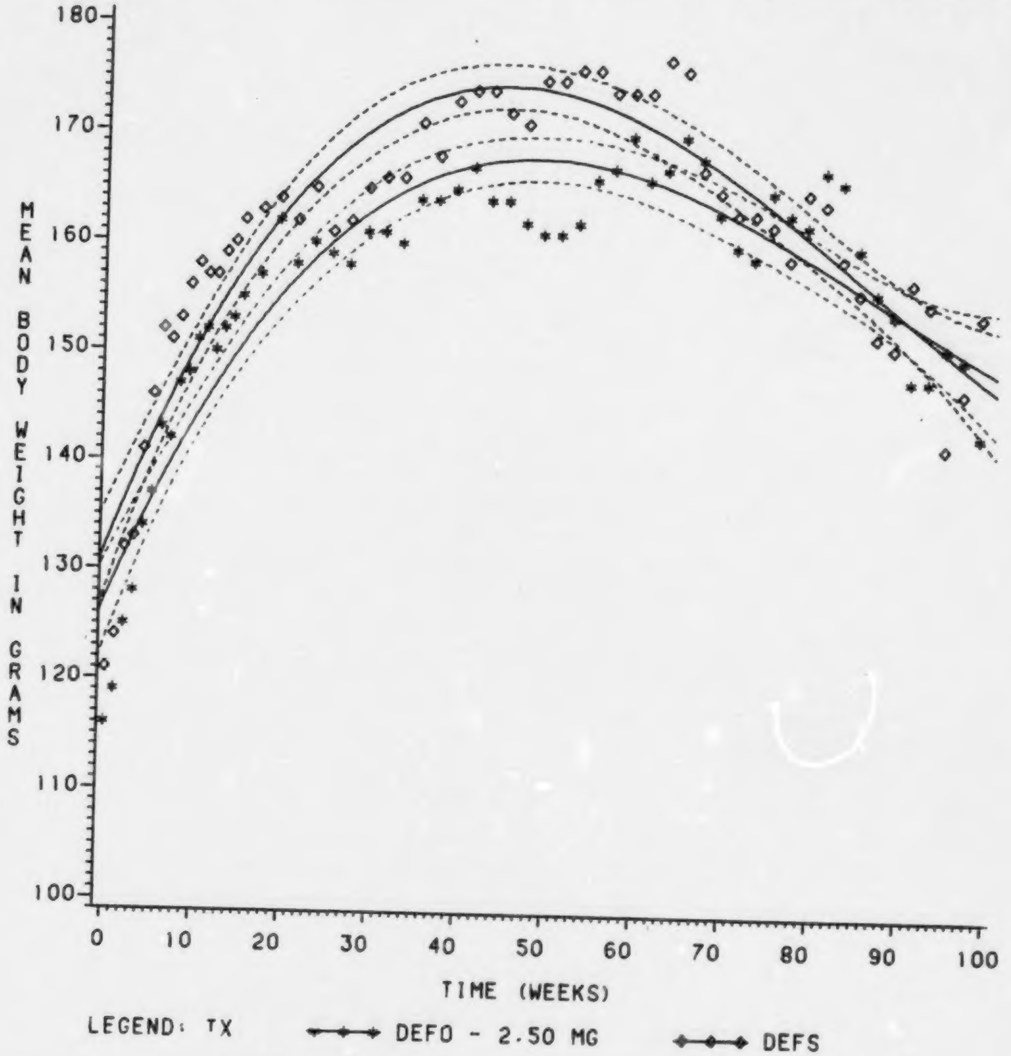
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DEFO(MEDIUM DOSE) AND DEFS

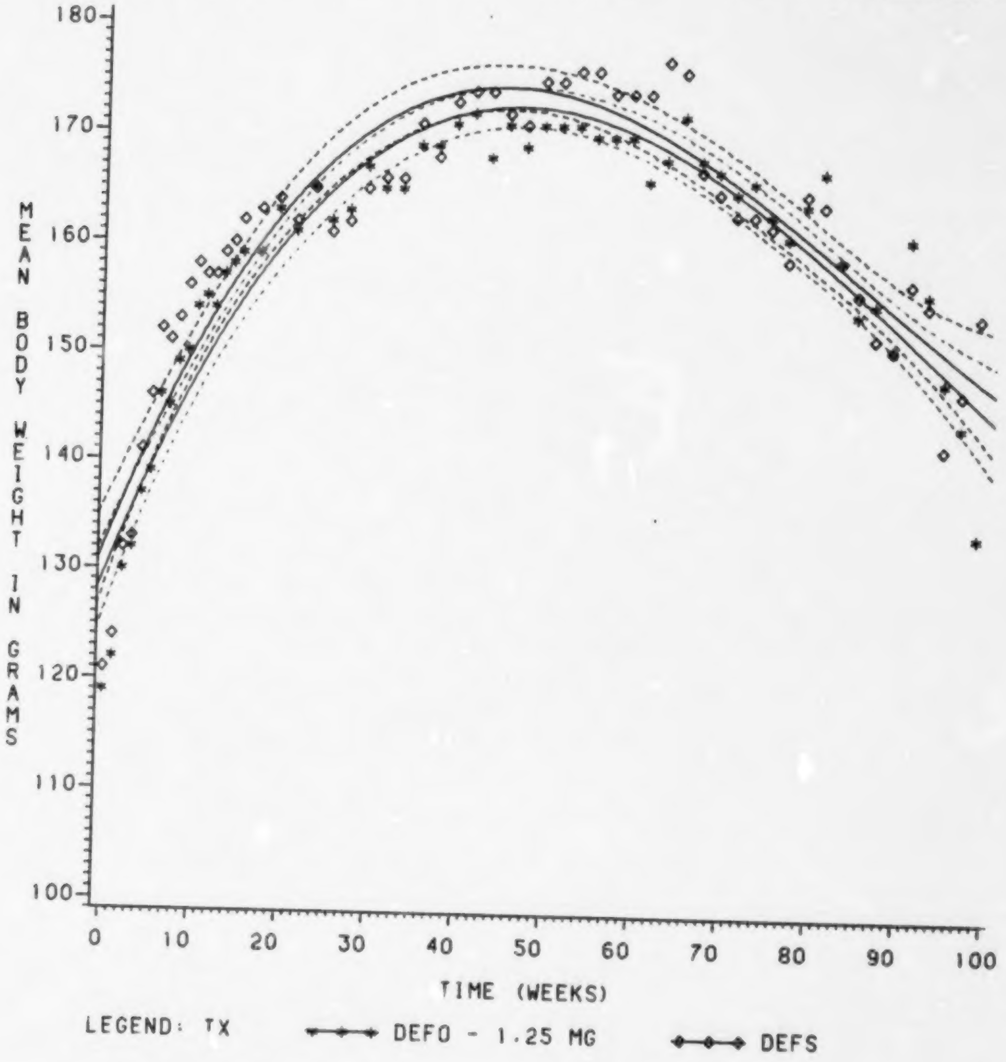
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DEFO(LOW DOSE) AND DEFS

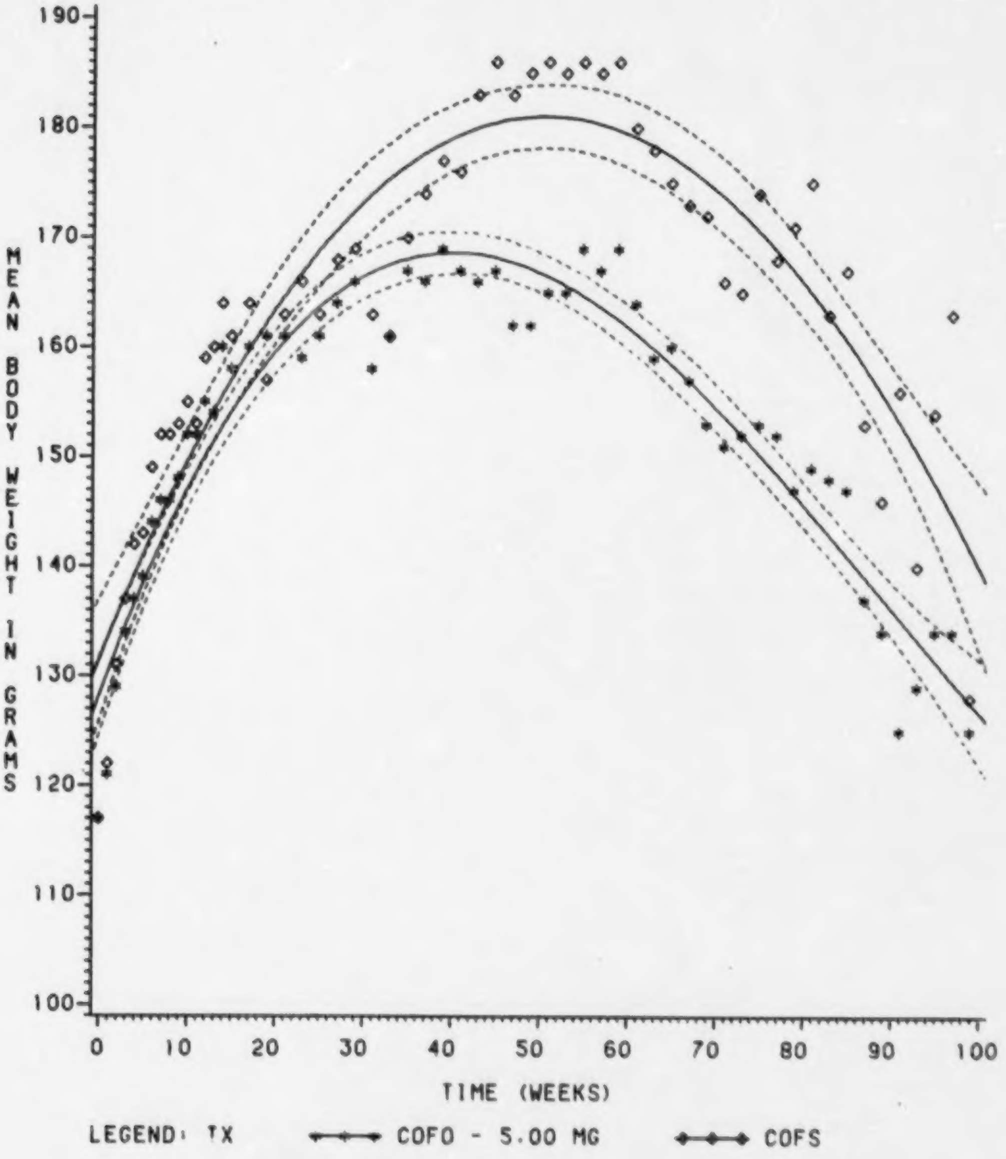
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

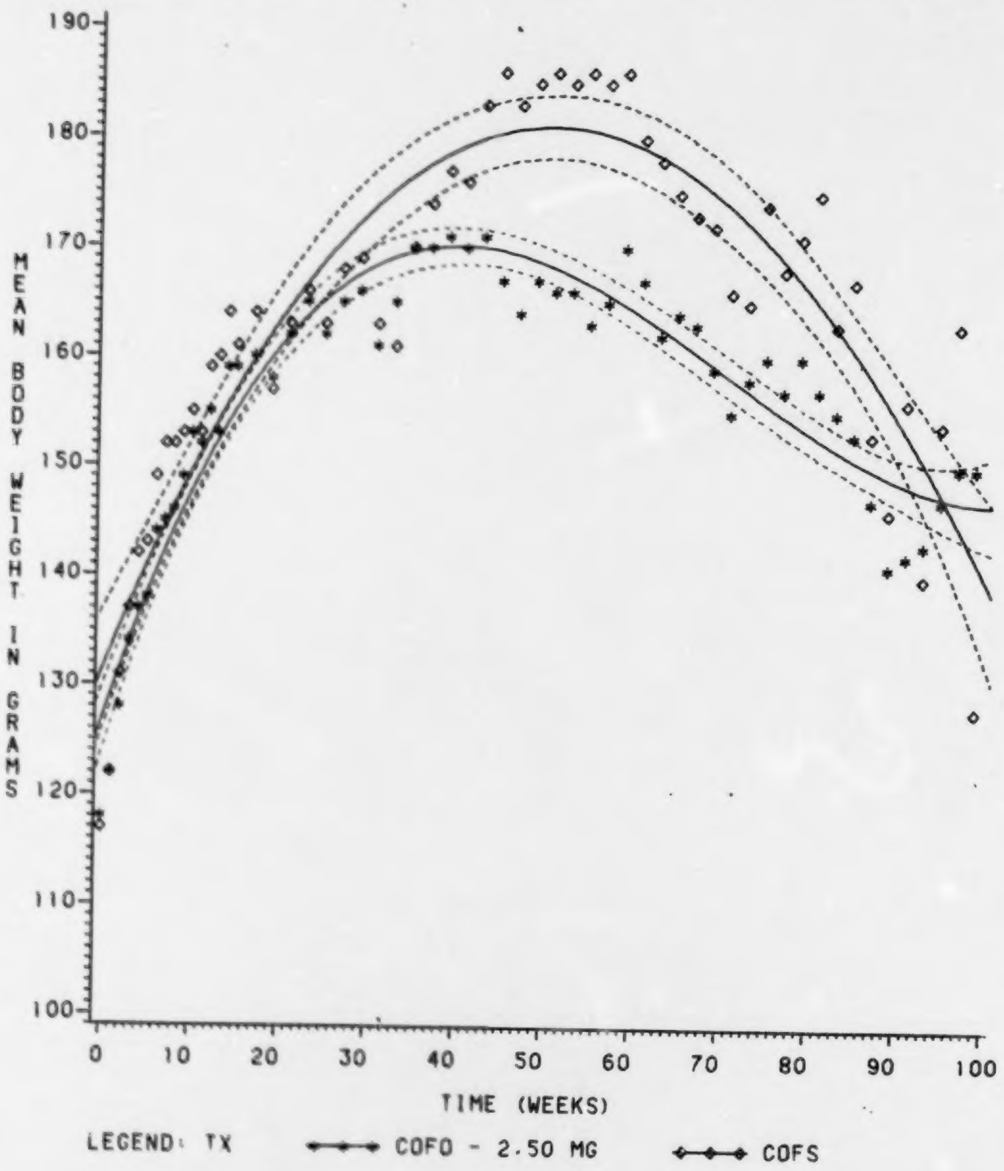
COMPOUND COFO(HIGH DOSE) AND COFS

MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

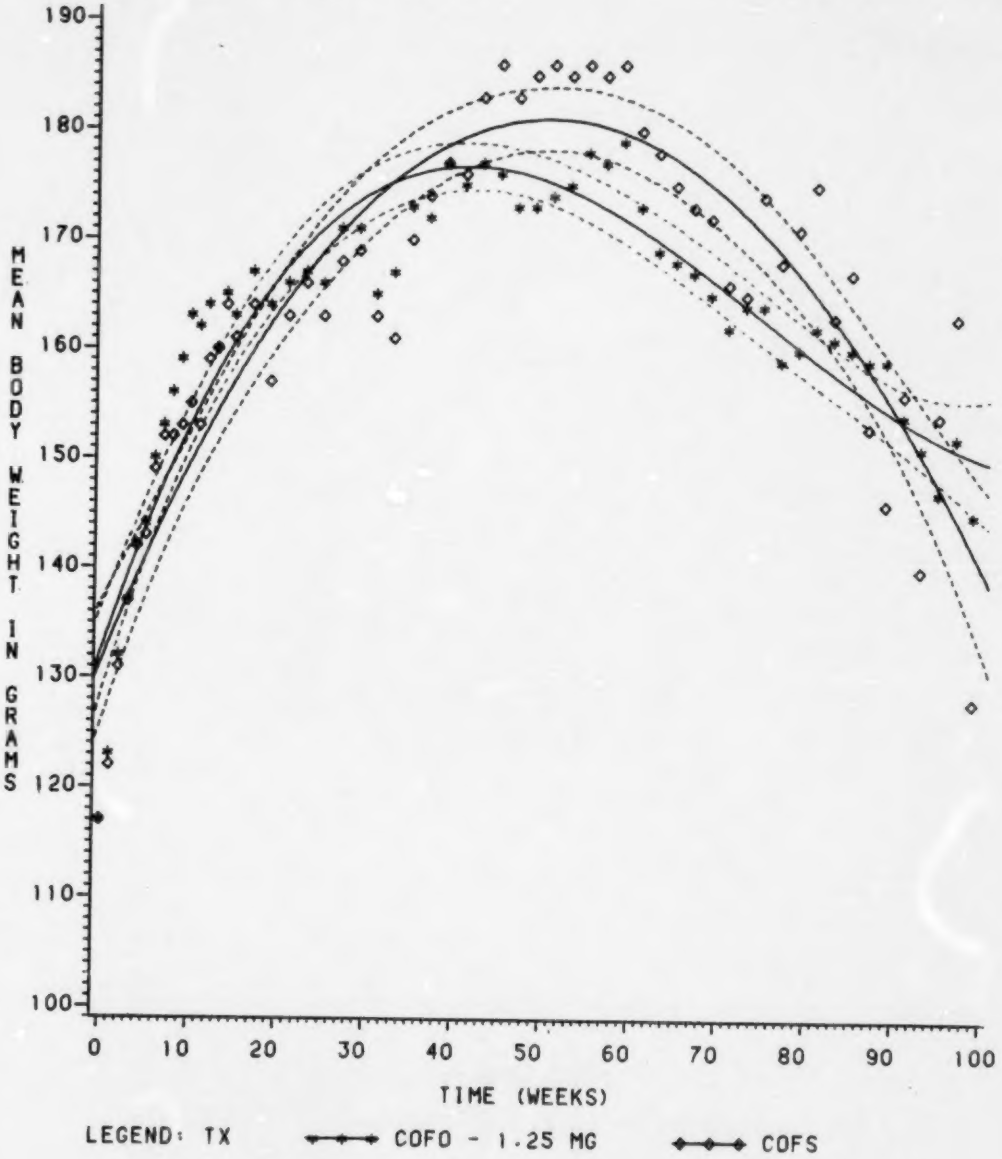
COMPOUND COFO(MEDIUM DOSE) AND COFS
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

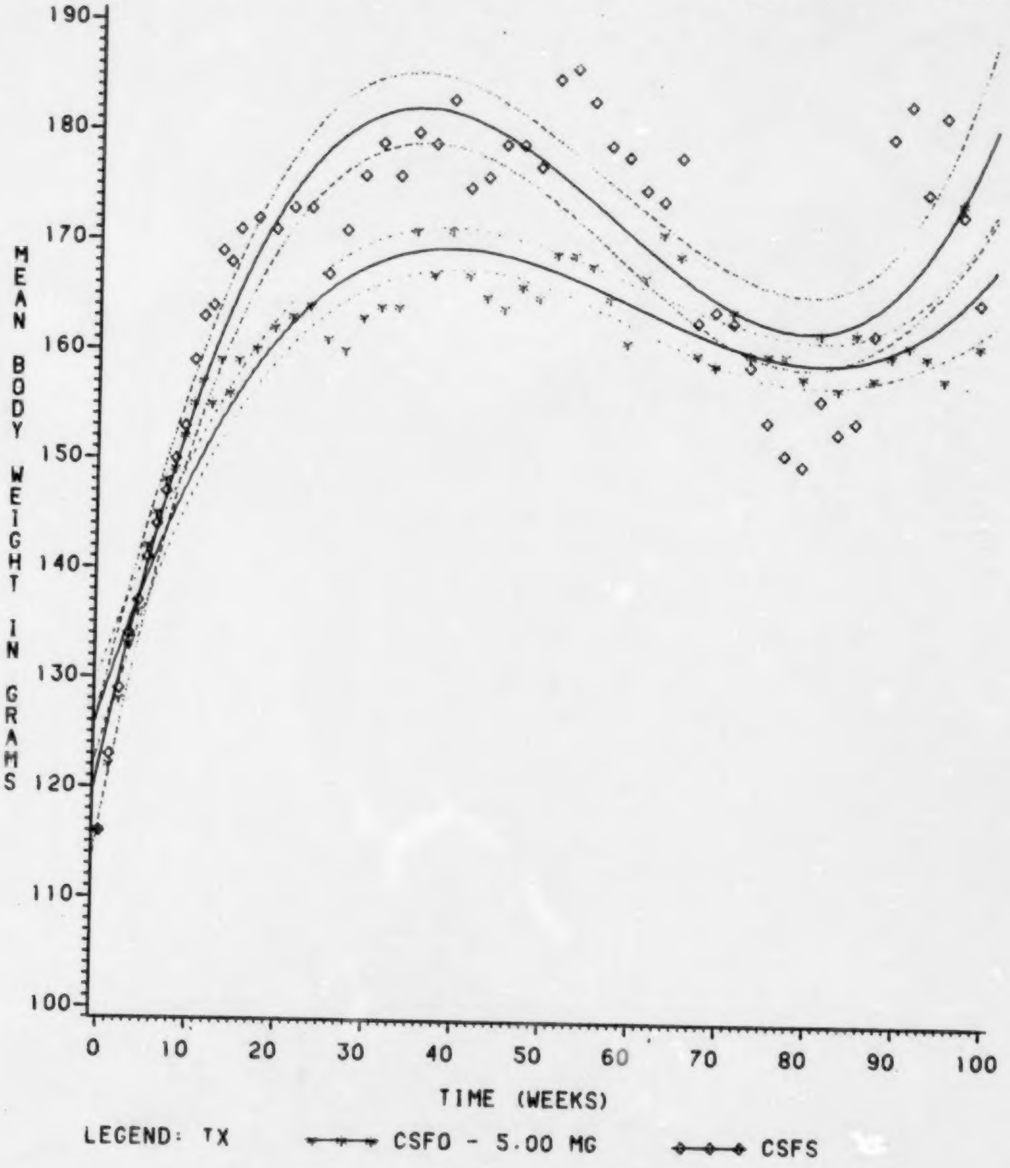
COMPOUND COFO(LOW DOSE) AND COFS

MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

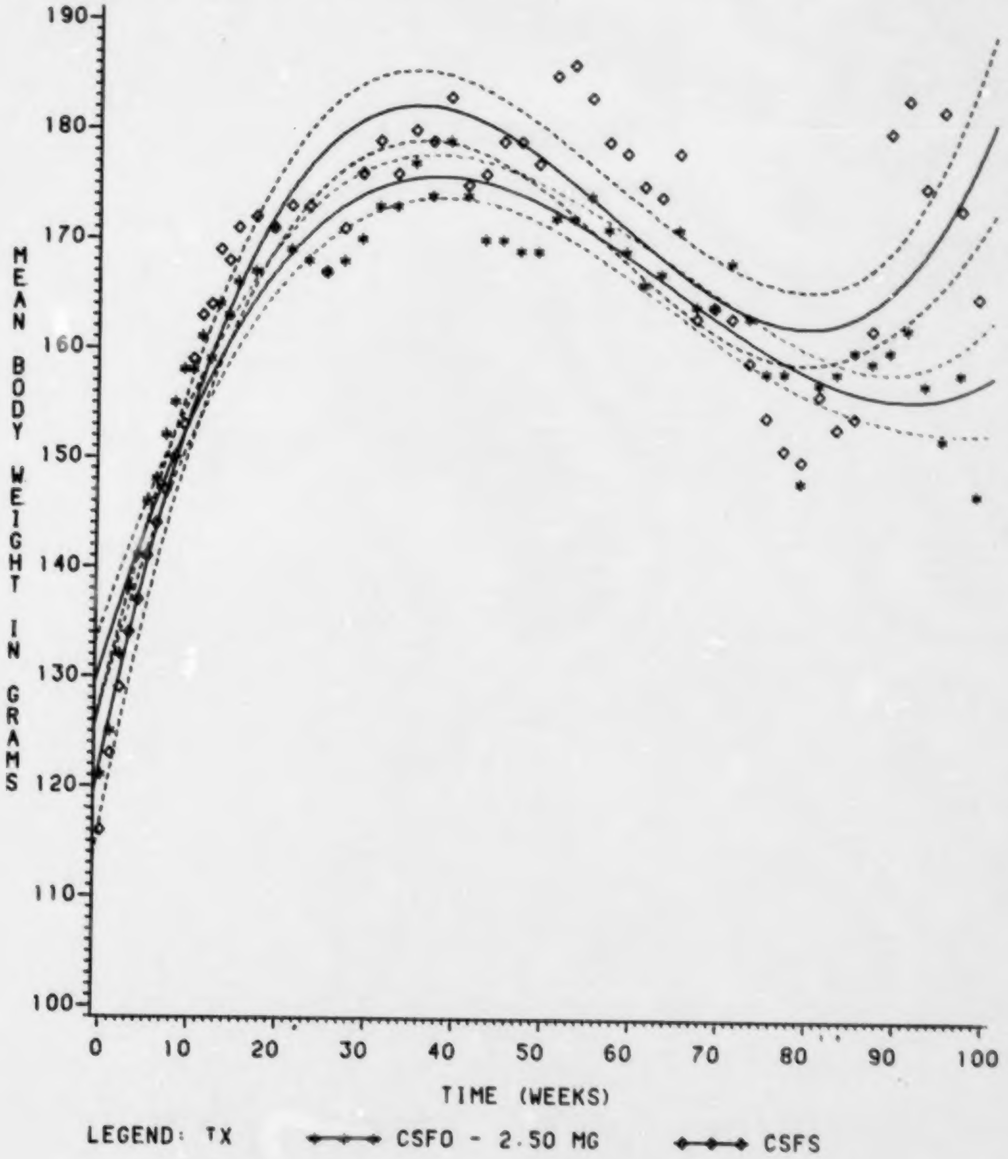
COMPOUND CSFO(HIGH DOSE) AND CSFS
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND CSFO(MEDIUM DOSE) AND CSFS

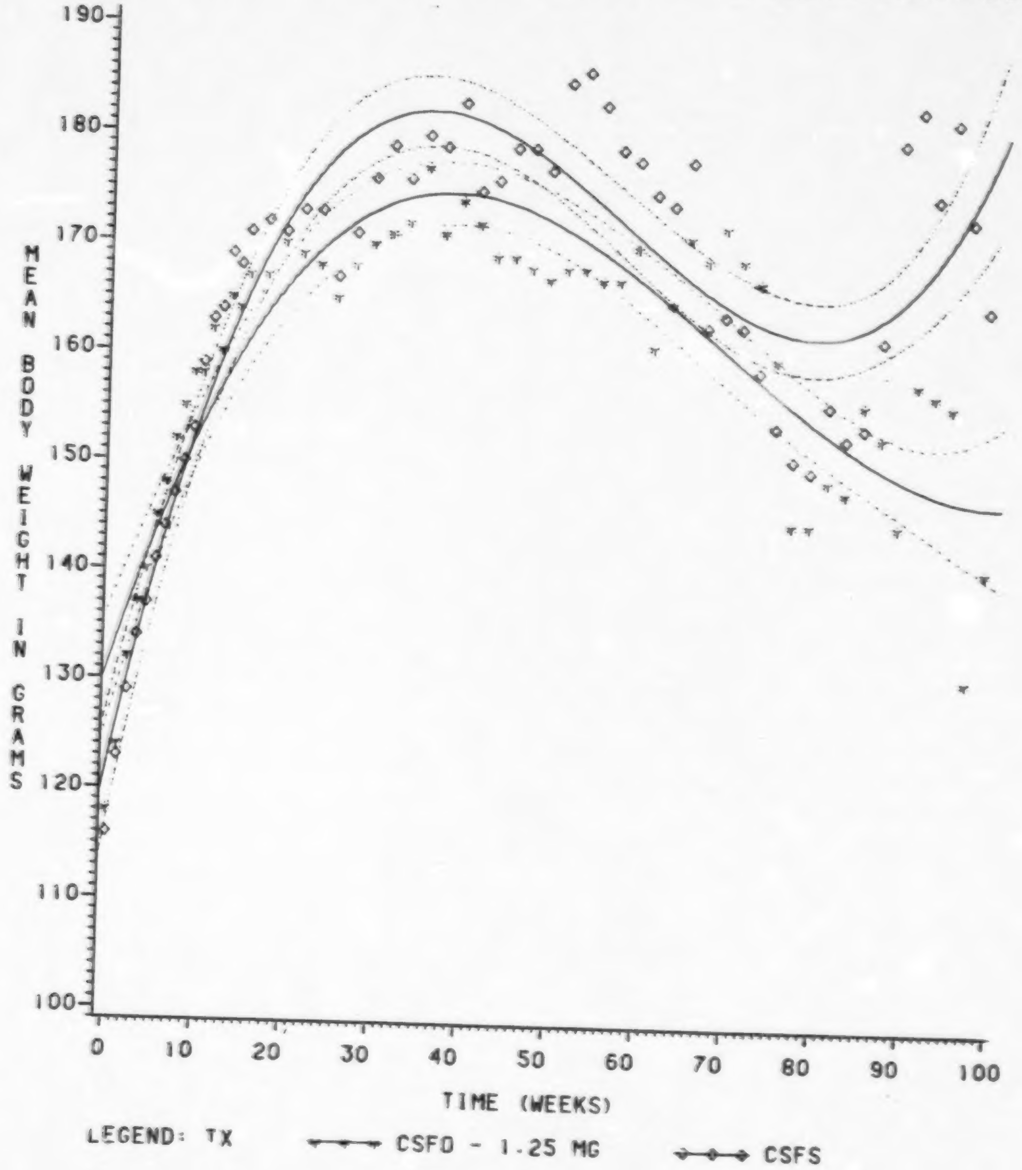
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

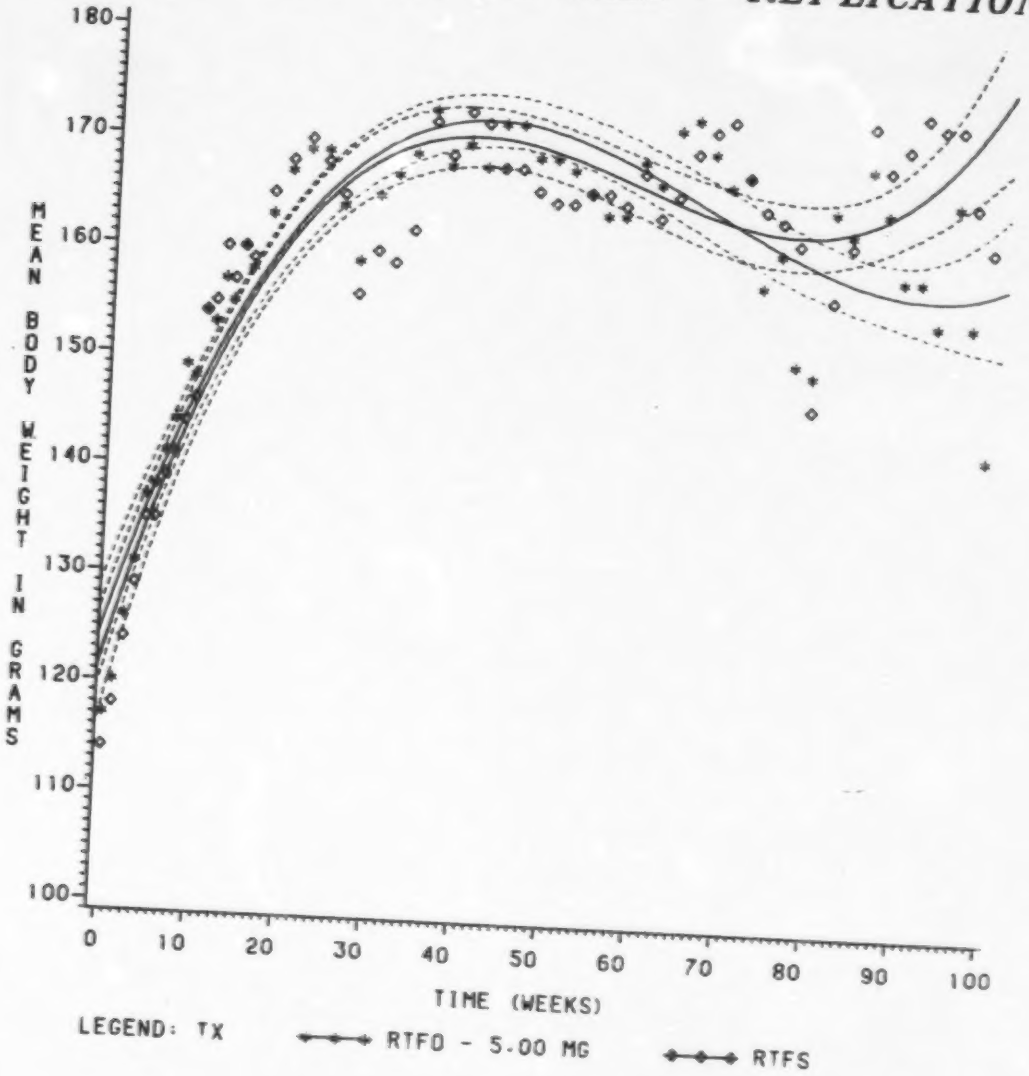
COMPOUND CSFO(LOW DOSE) AND CSFS

MEAN BODY WEIGHT VS TIME – REPLICATION 1



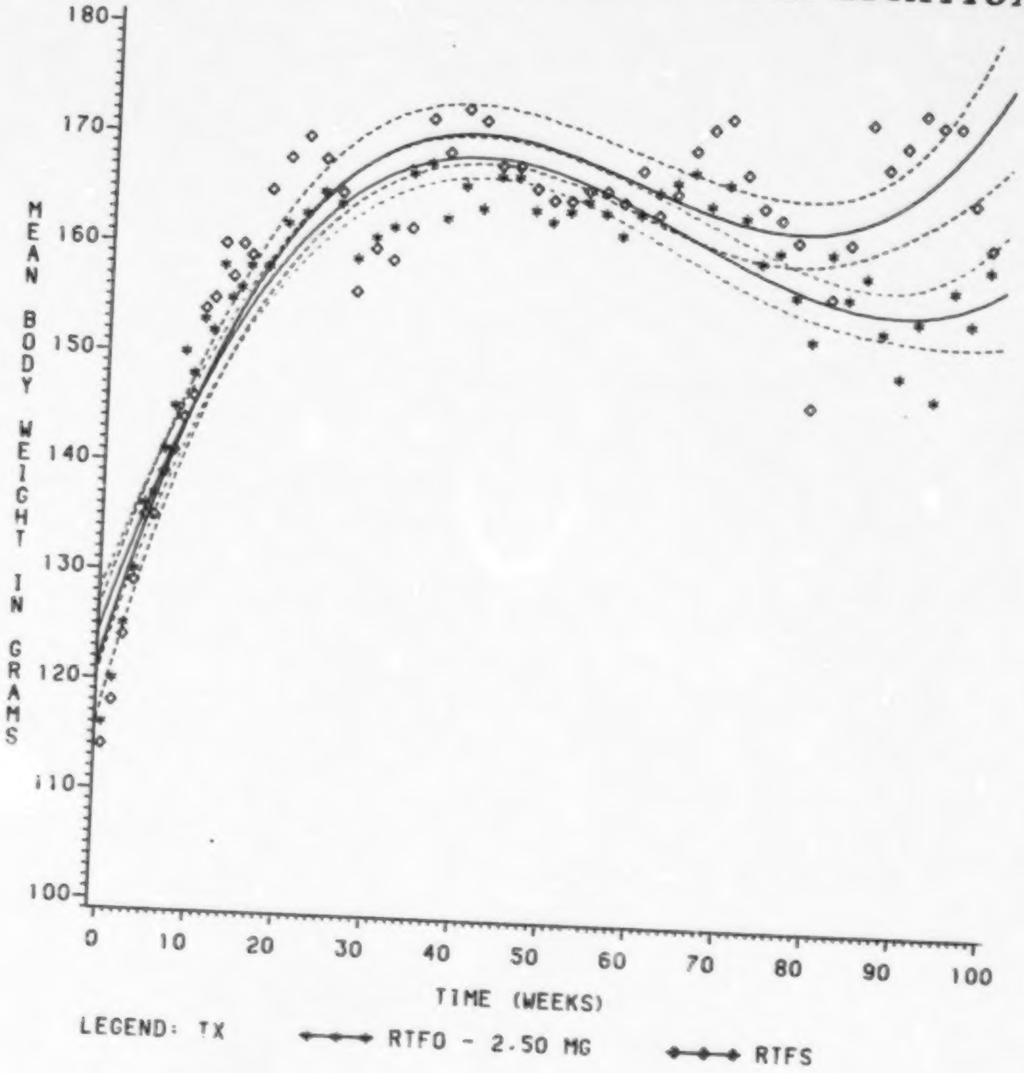
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND RTFO(HIGH DOSE) AND RTFS
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

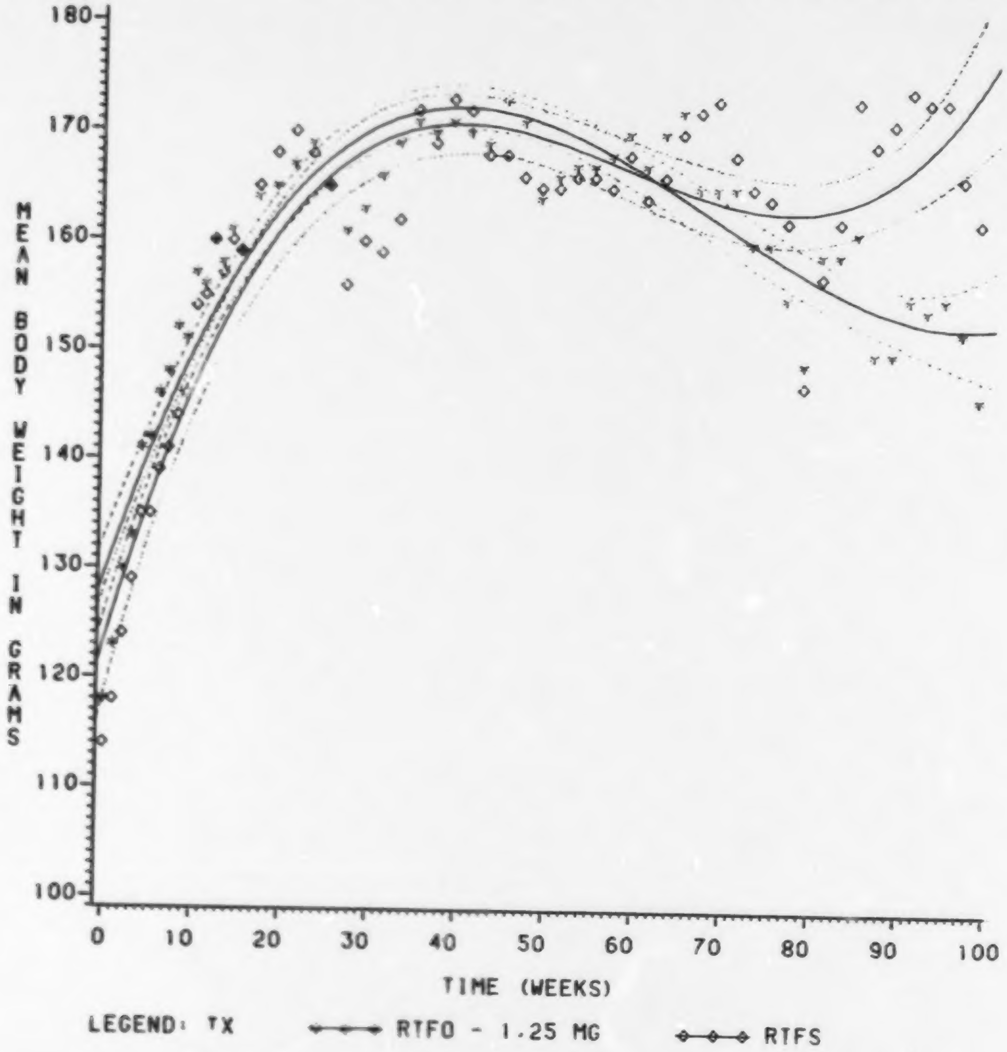
COMPOUND RTFO(MEDIUM DOSE) AND RTFS
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

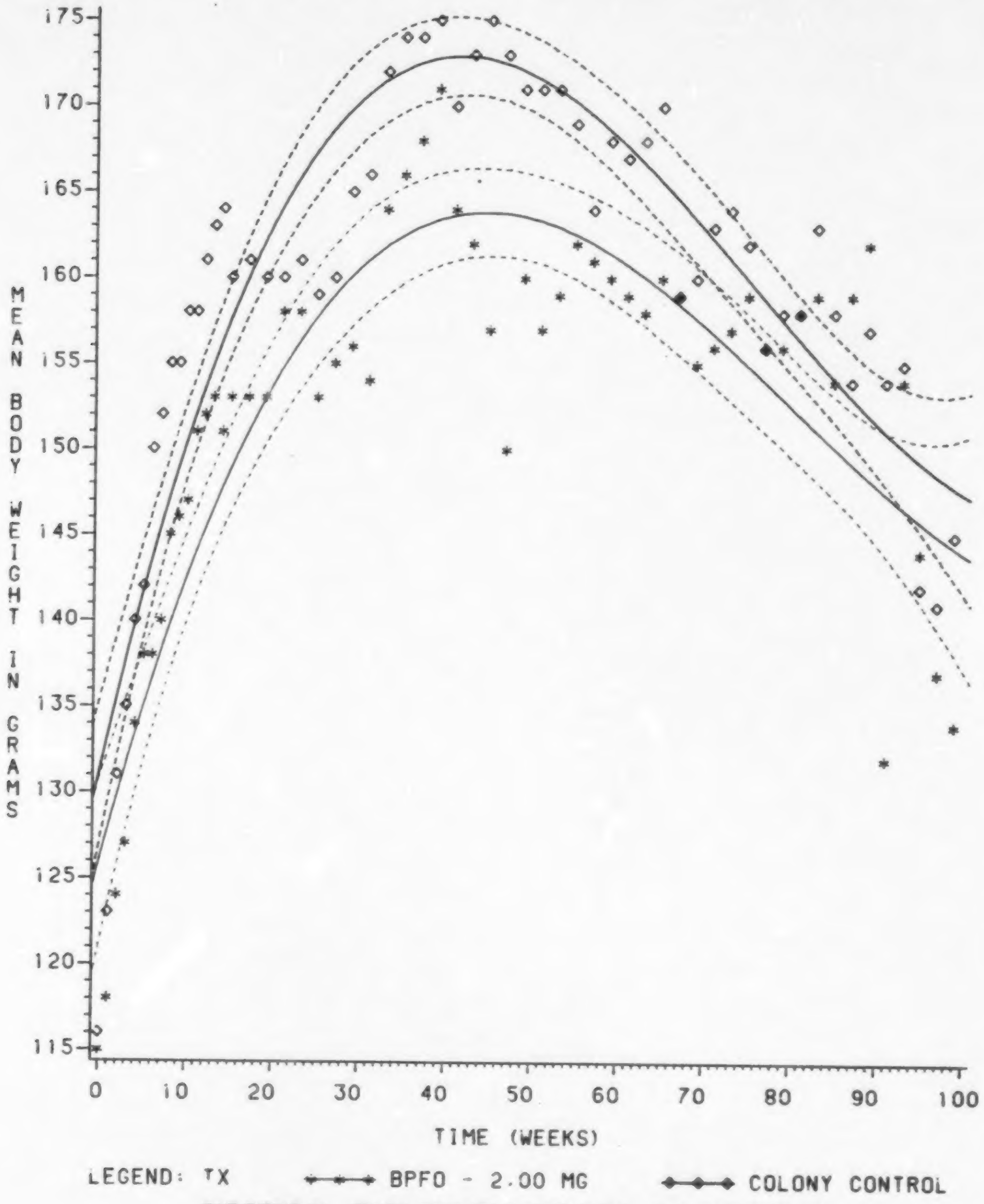
COMPOUND RTFO(LOW DOSE) AND RTFS

MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

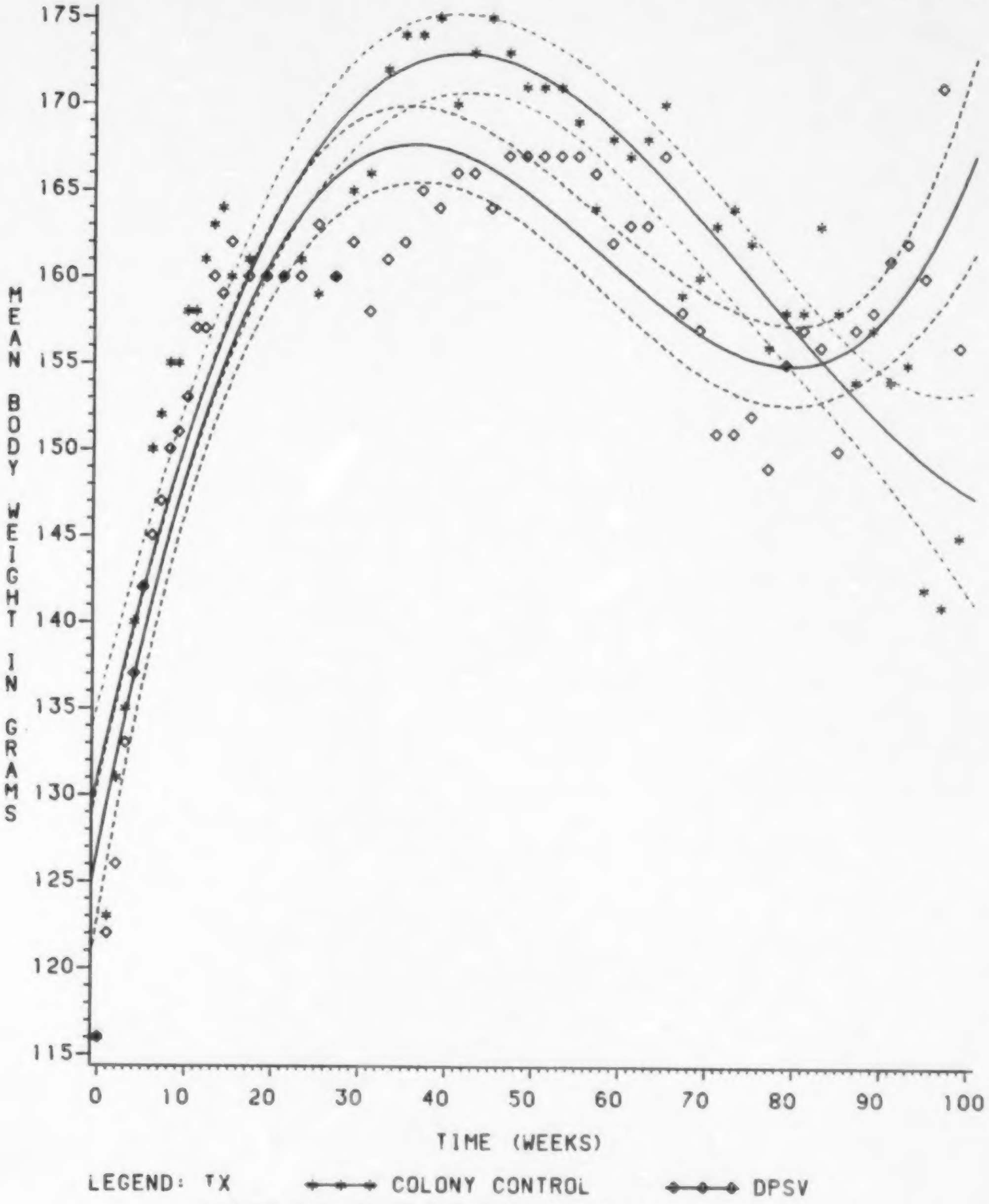
COMPOUND BPFO AND COLONY CONTROL
MEAN BODY WEIGHT VS TIME – REPLICATION 1



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DPSV AND COLONY CONTROL

MEAN BODY WEIGHT VS TIME – REPLICATION 1

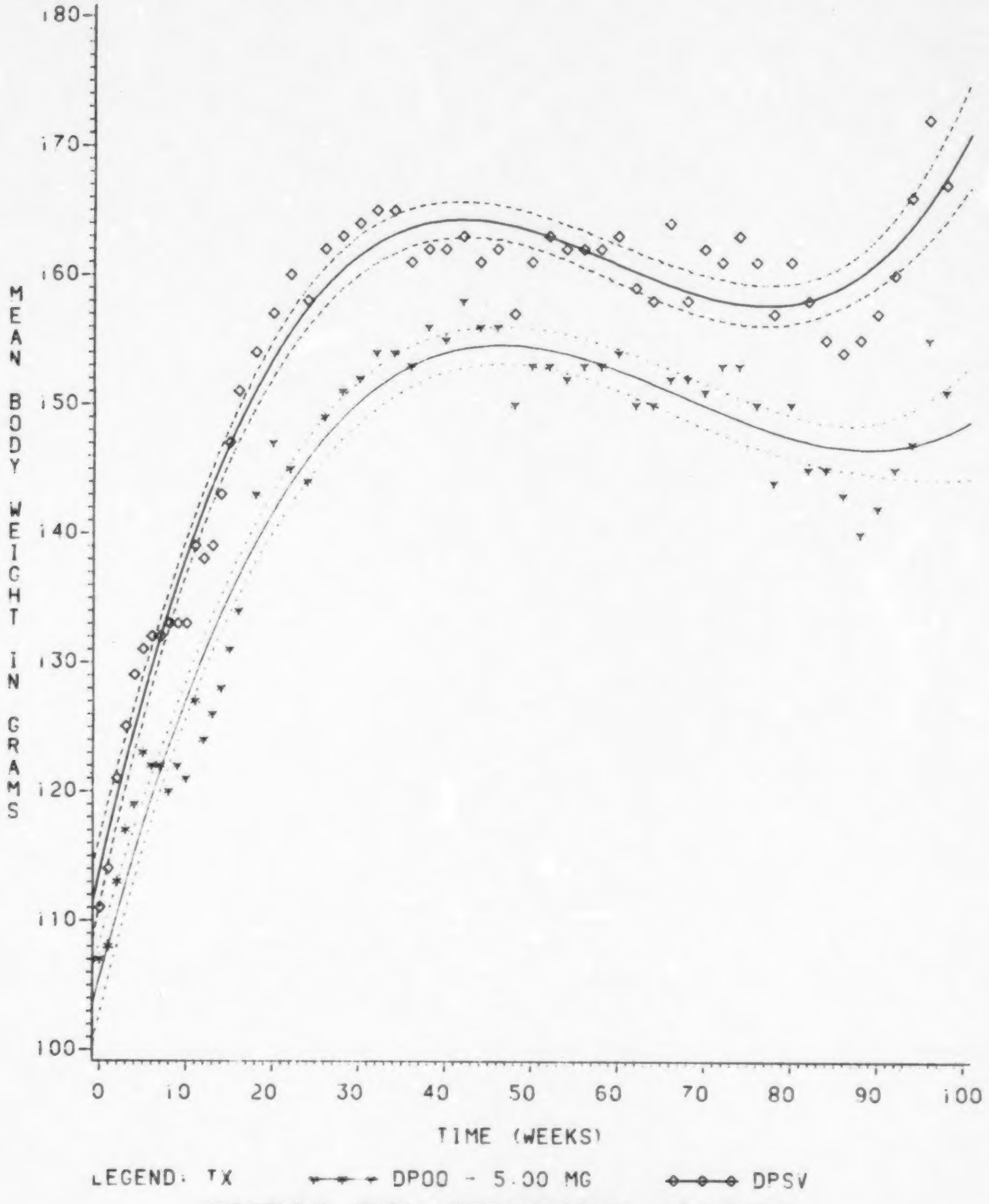


CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

F.2 Second Replicate

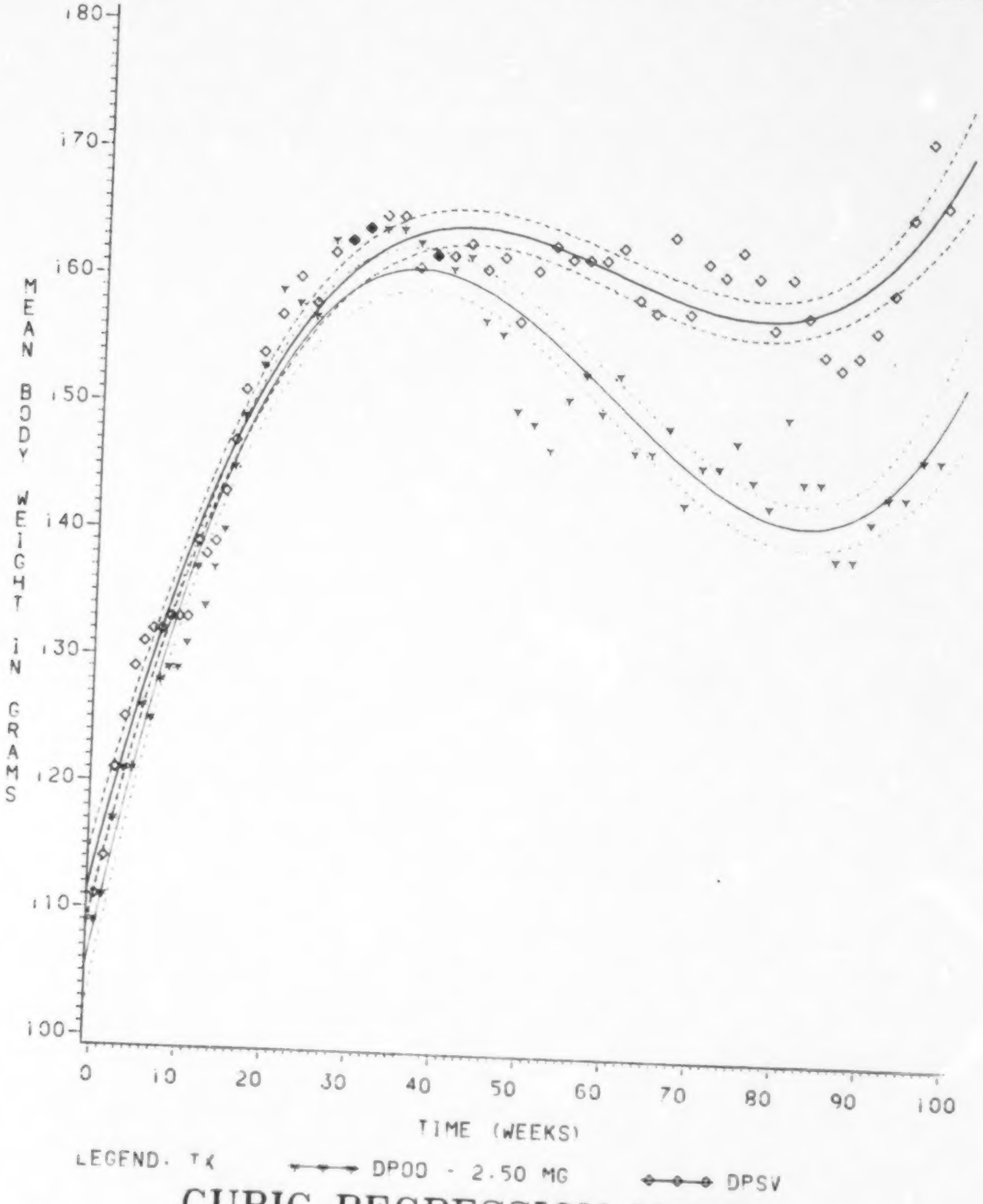
COMPOUND DPOO(HIGH DOSE) AND DPSV

MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

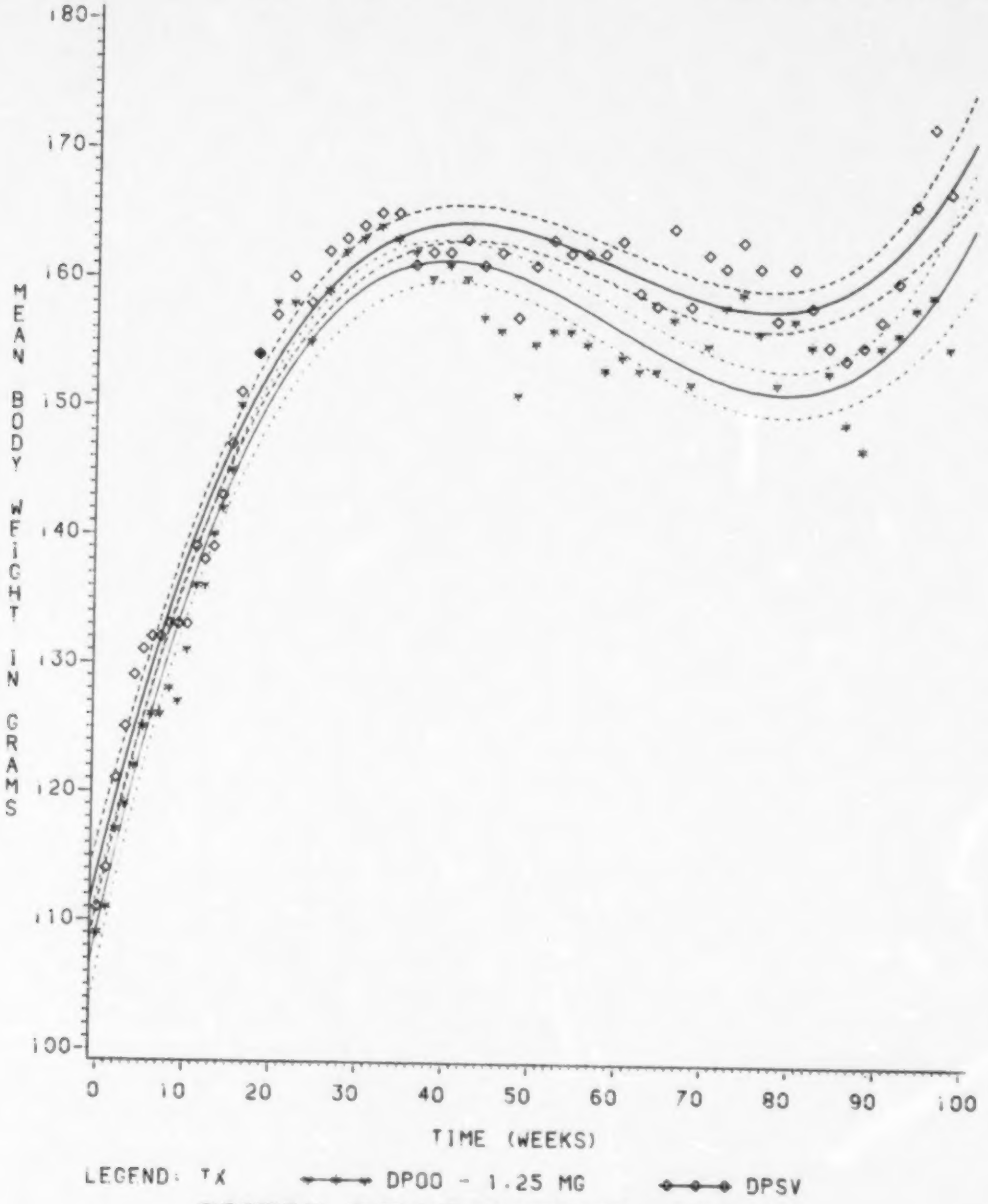
COMPOUND DPOO(MEDIUM DOSE) AND DPSV
MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

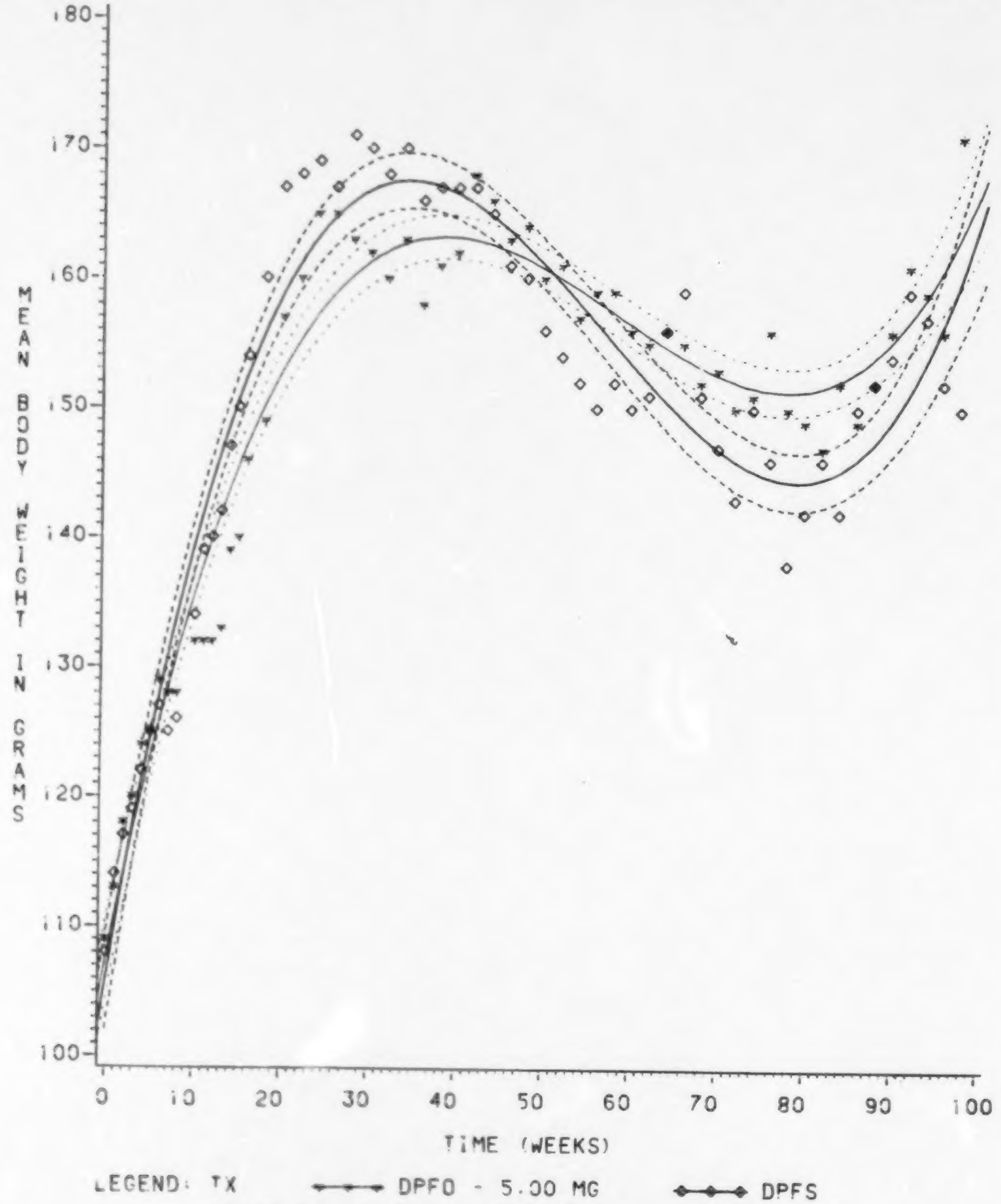
COMPOUND DPOO(LOW DOSE) AND DPSV

MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

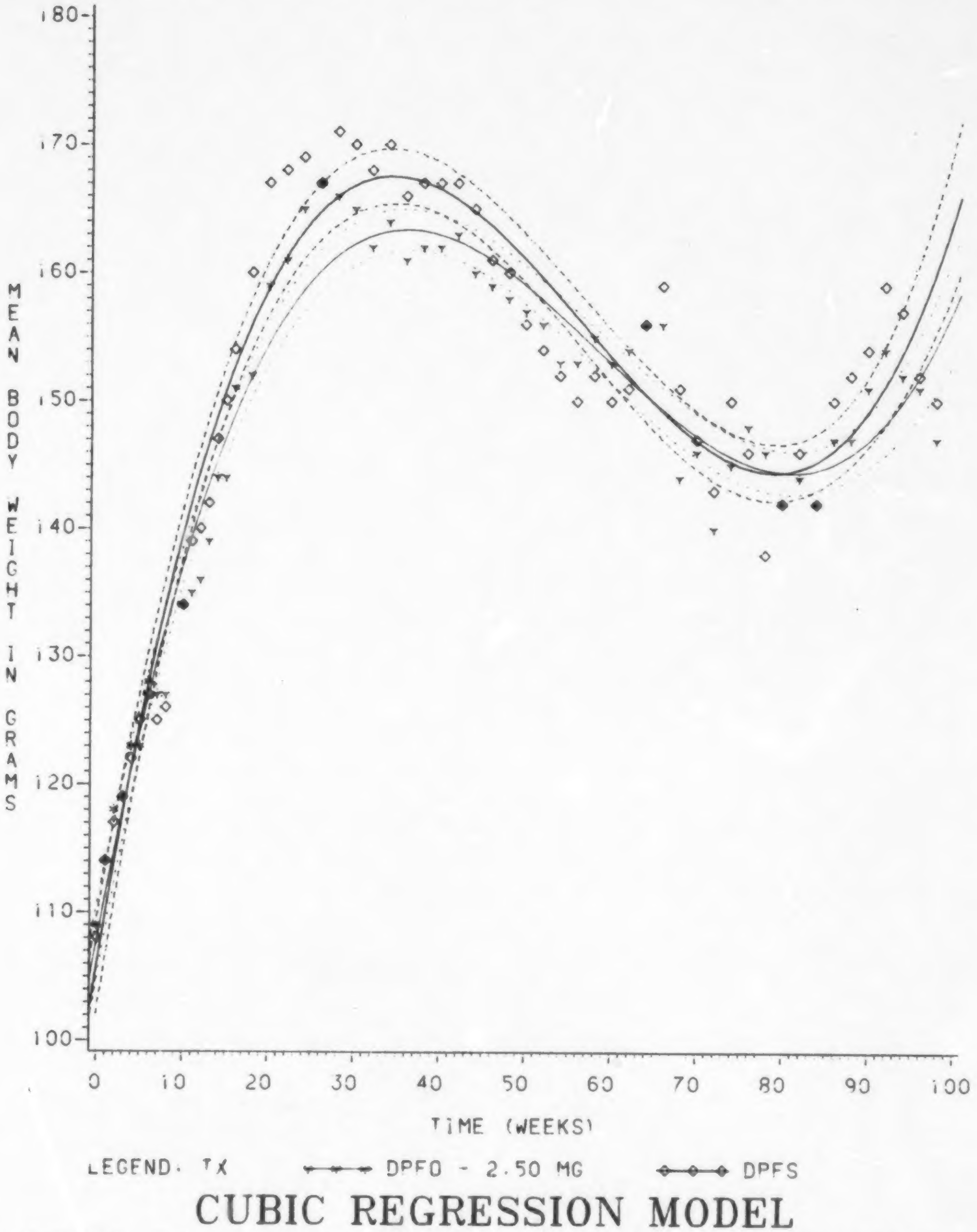
COMPOUND DPFO(HIGH DOSE) AND DPFS
MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DPFO(MEDIUM DOSE) AND DPFS

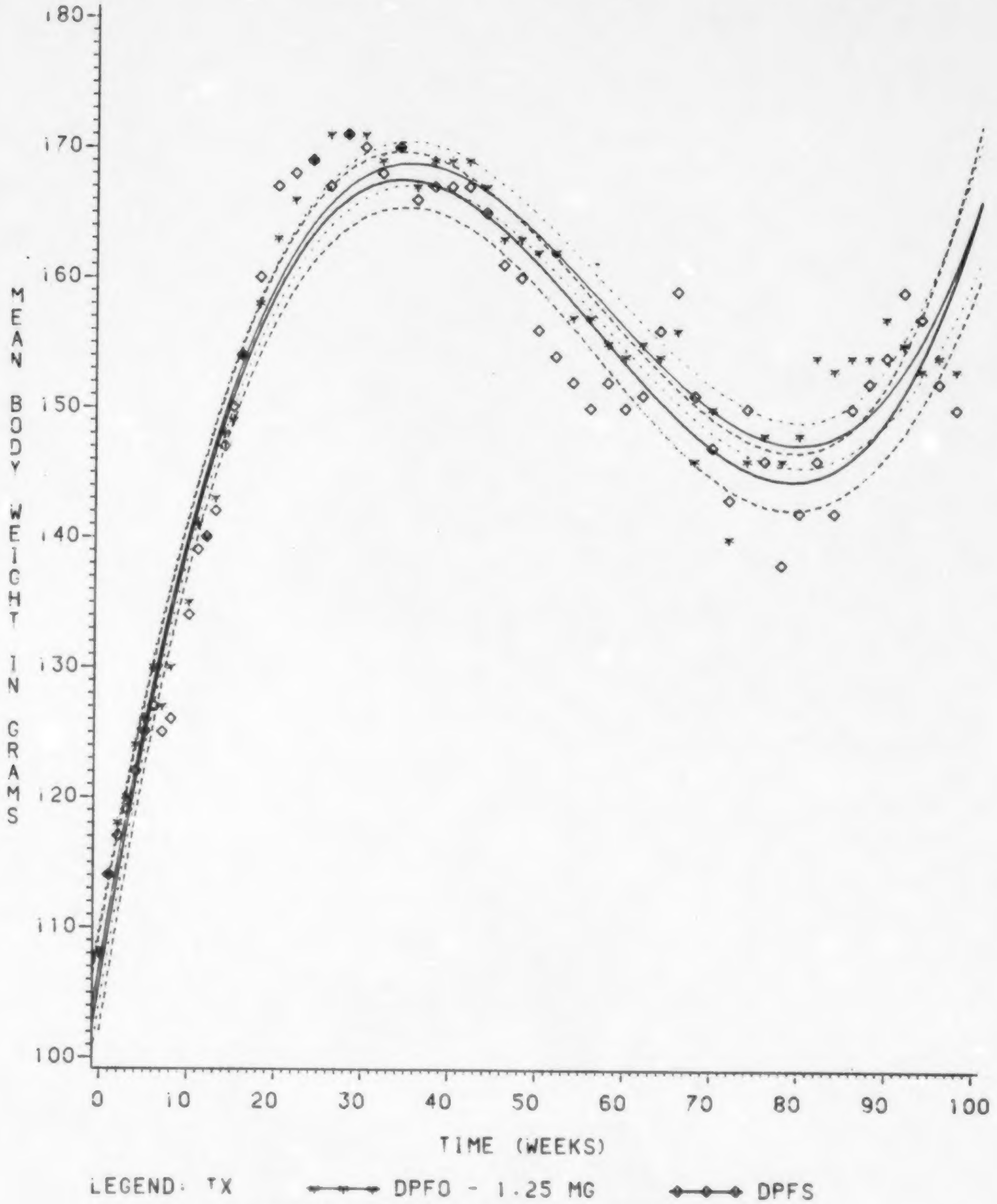
MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DPFO(LOW DOSE) AND DPFS

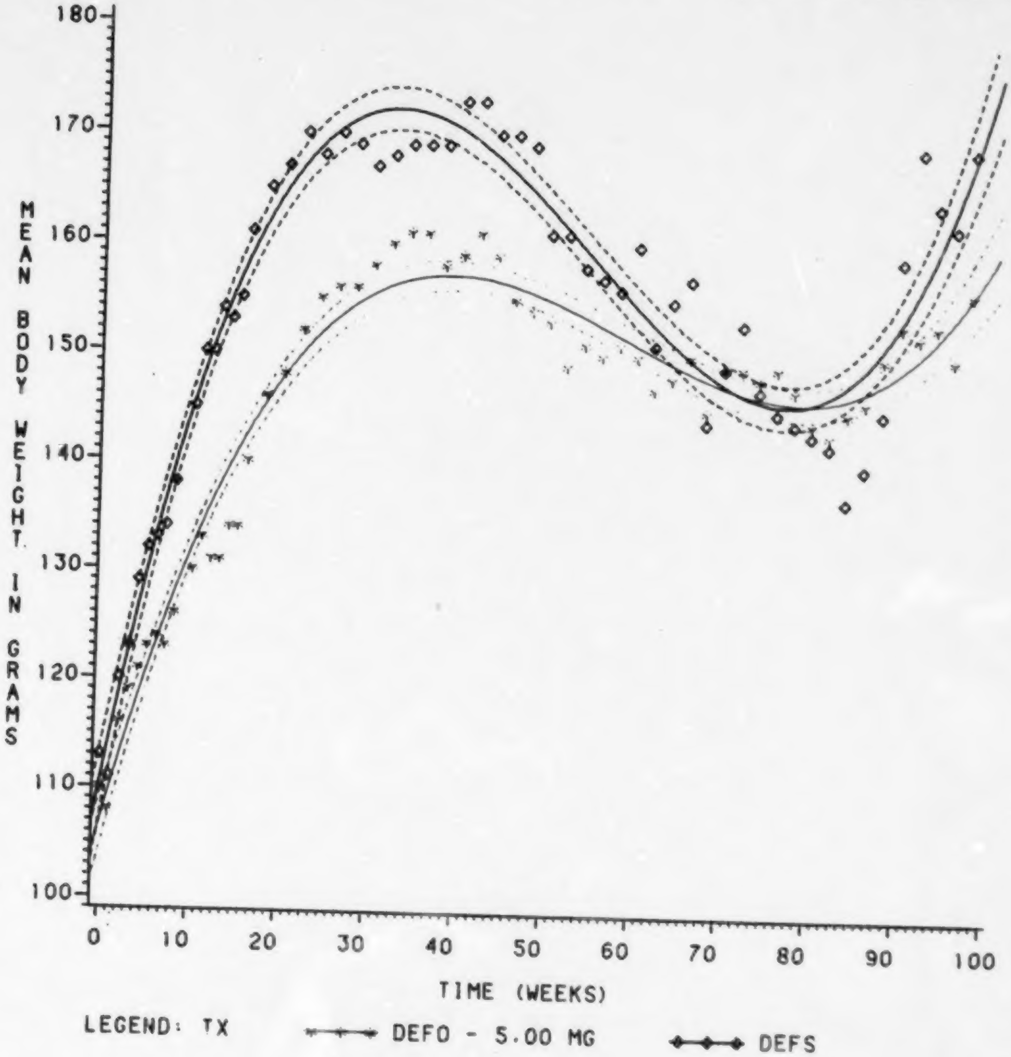
MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

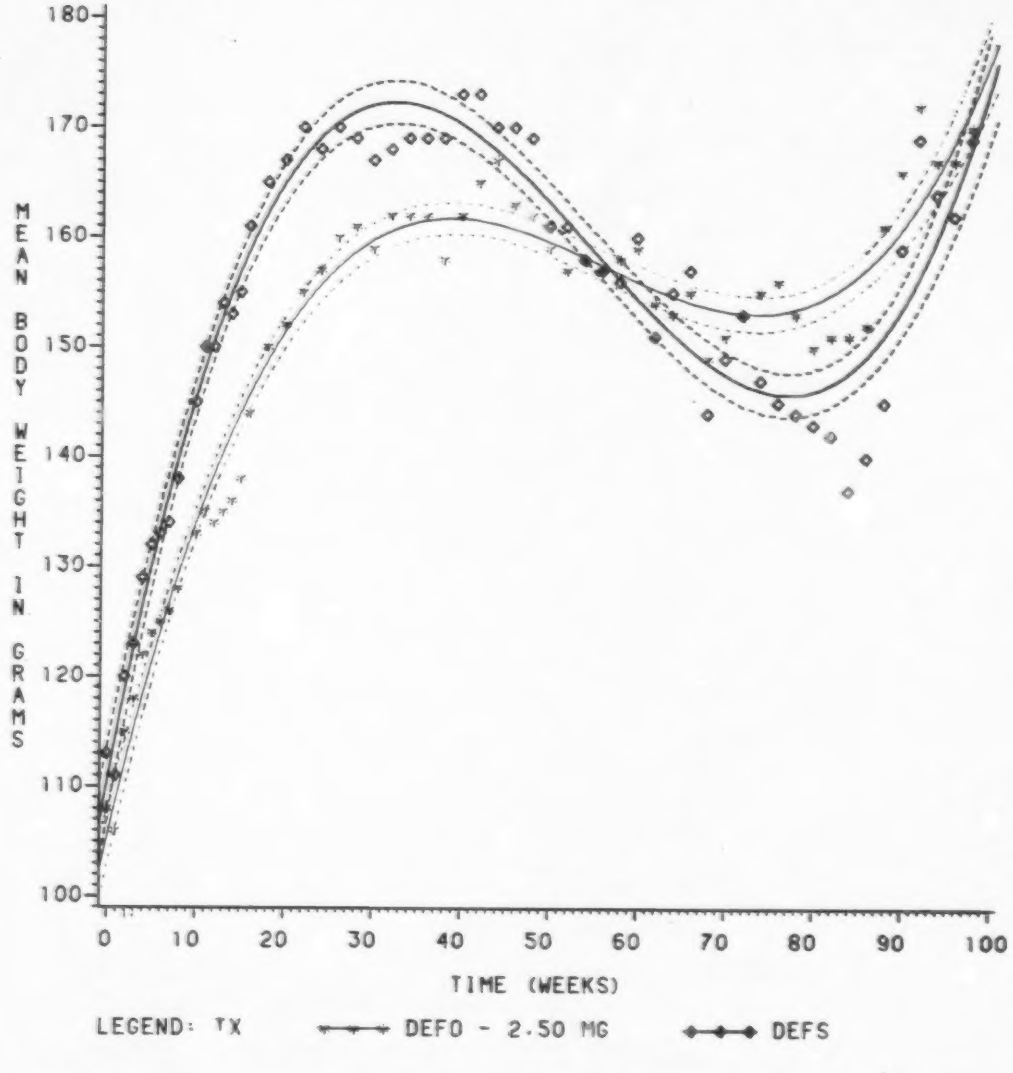
COMPOUND DEFO(HIGH DOSE) AND DEFS

MEAN BODY WEIGHT VS TIME - REPLICATION 2



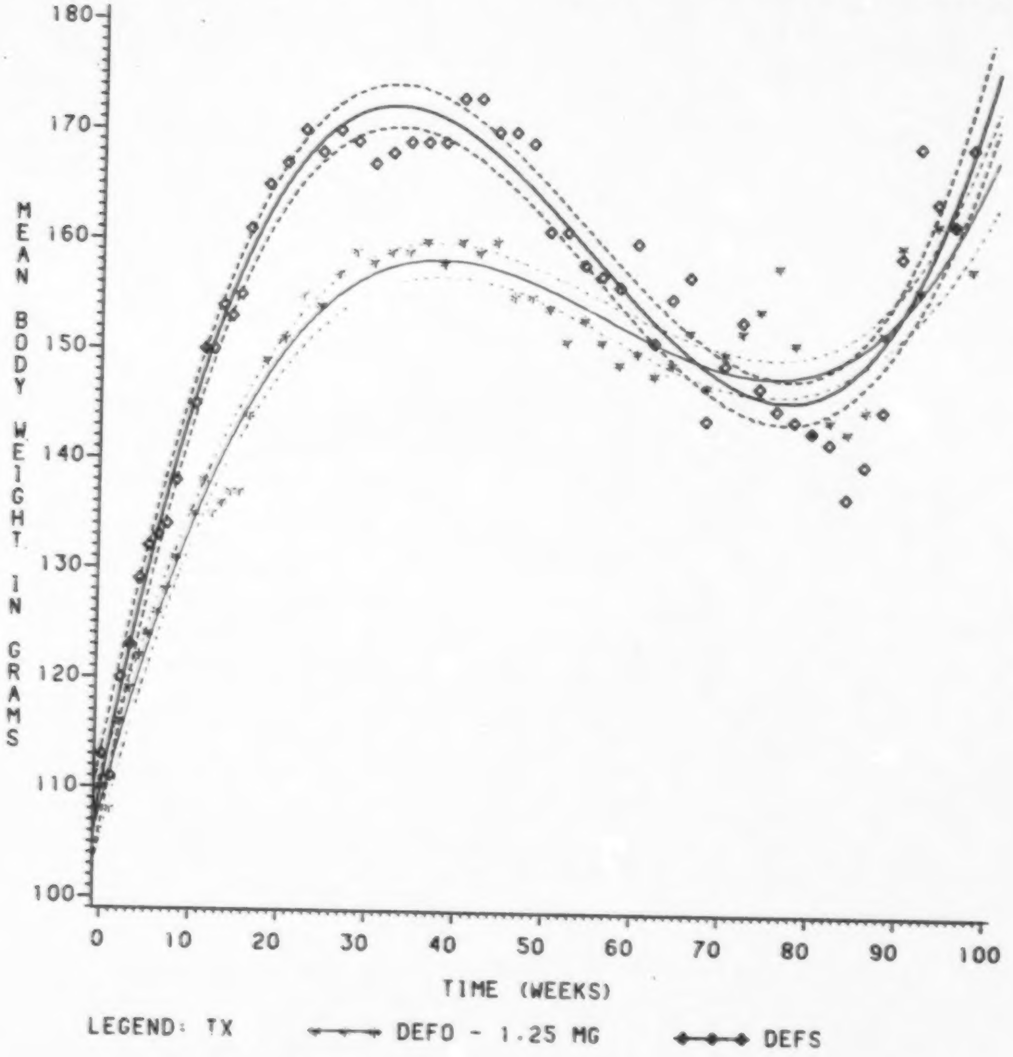
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DEFO(MEDIUM DOSE) AND DEFS
MEAN BODY WEIGHT VS TIME – REPLICATION 2



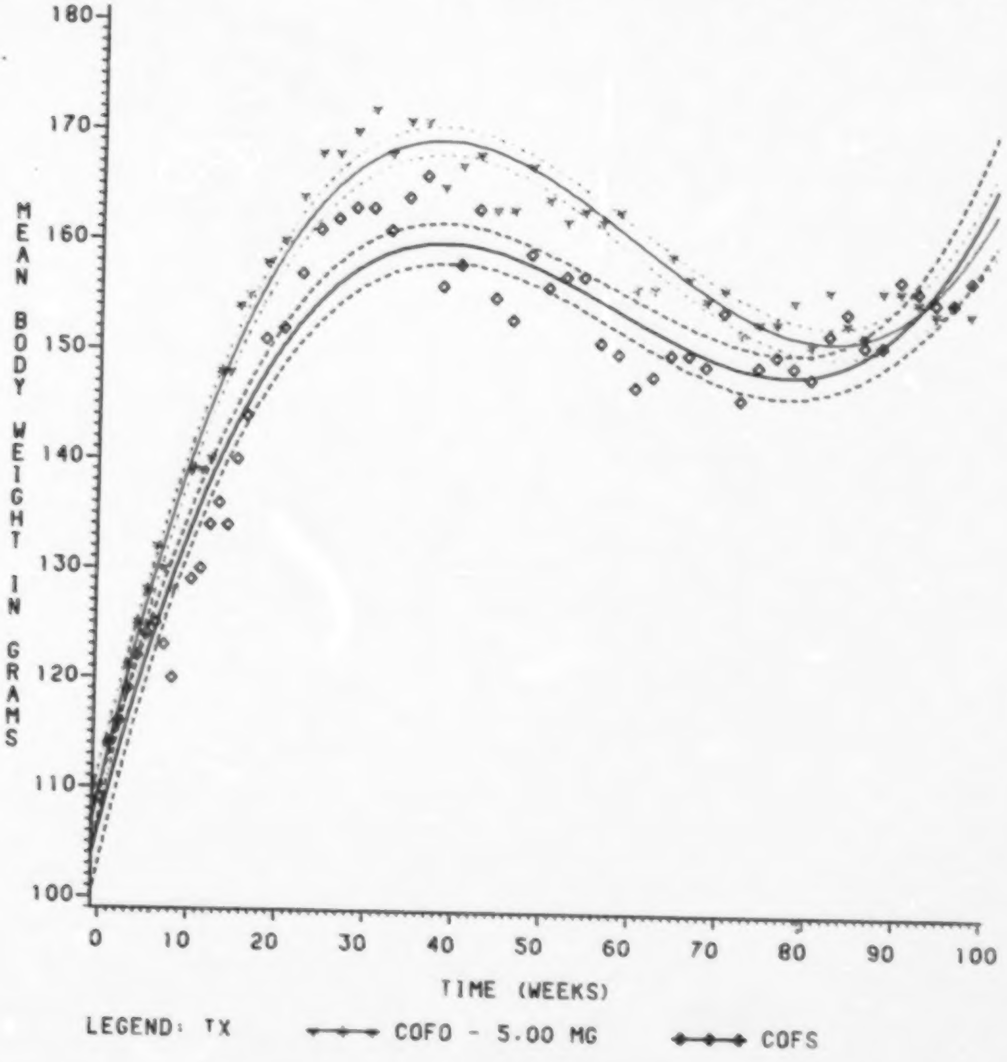
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DEFO(LOW DOSE) AND DEFS
MEAN BODY WEIGHT VS TIME – REPLICATION 2



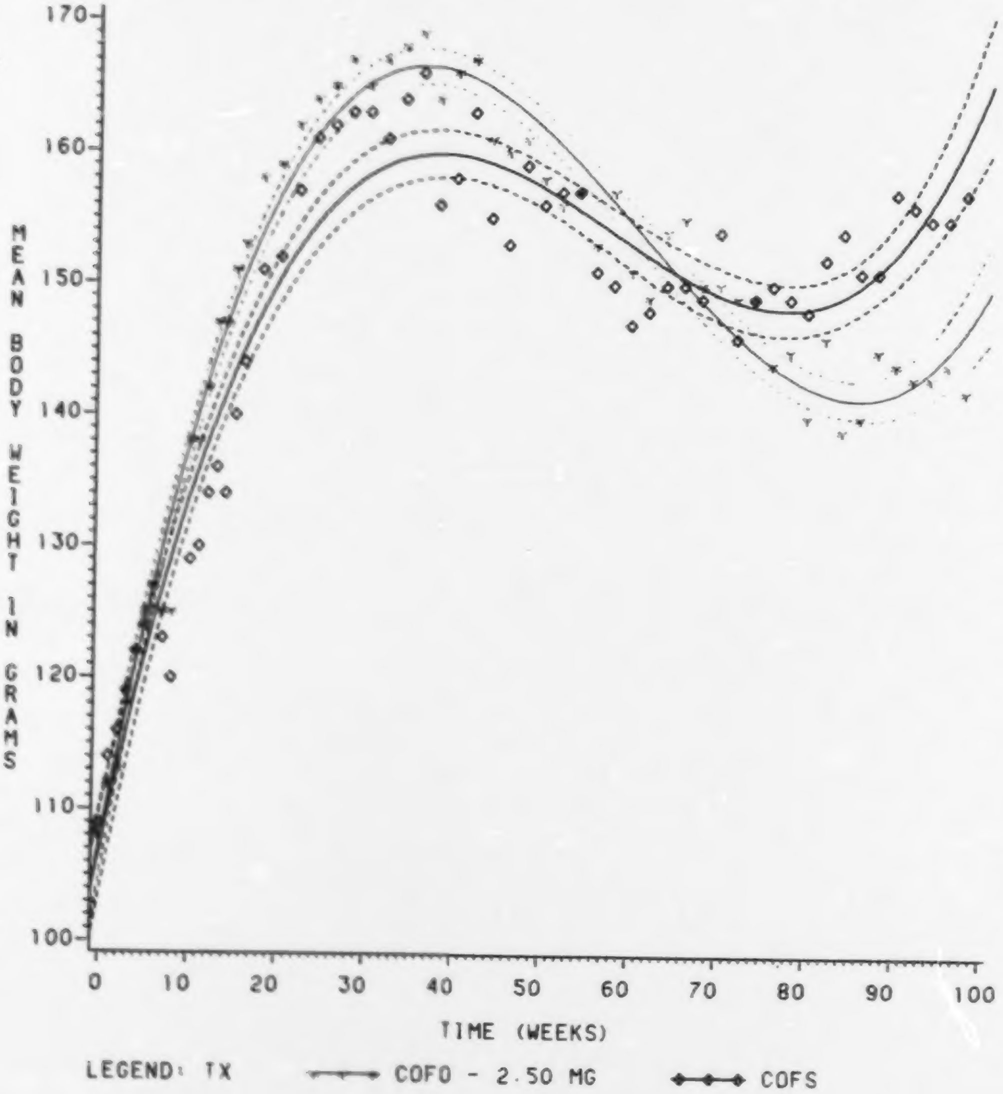
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND COFO(HIGH DOSE) AND COFS
MEAN BODY WEIGHT VS TIME – REPLICATION 2



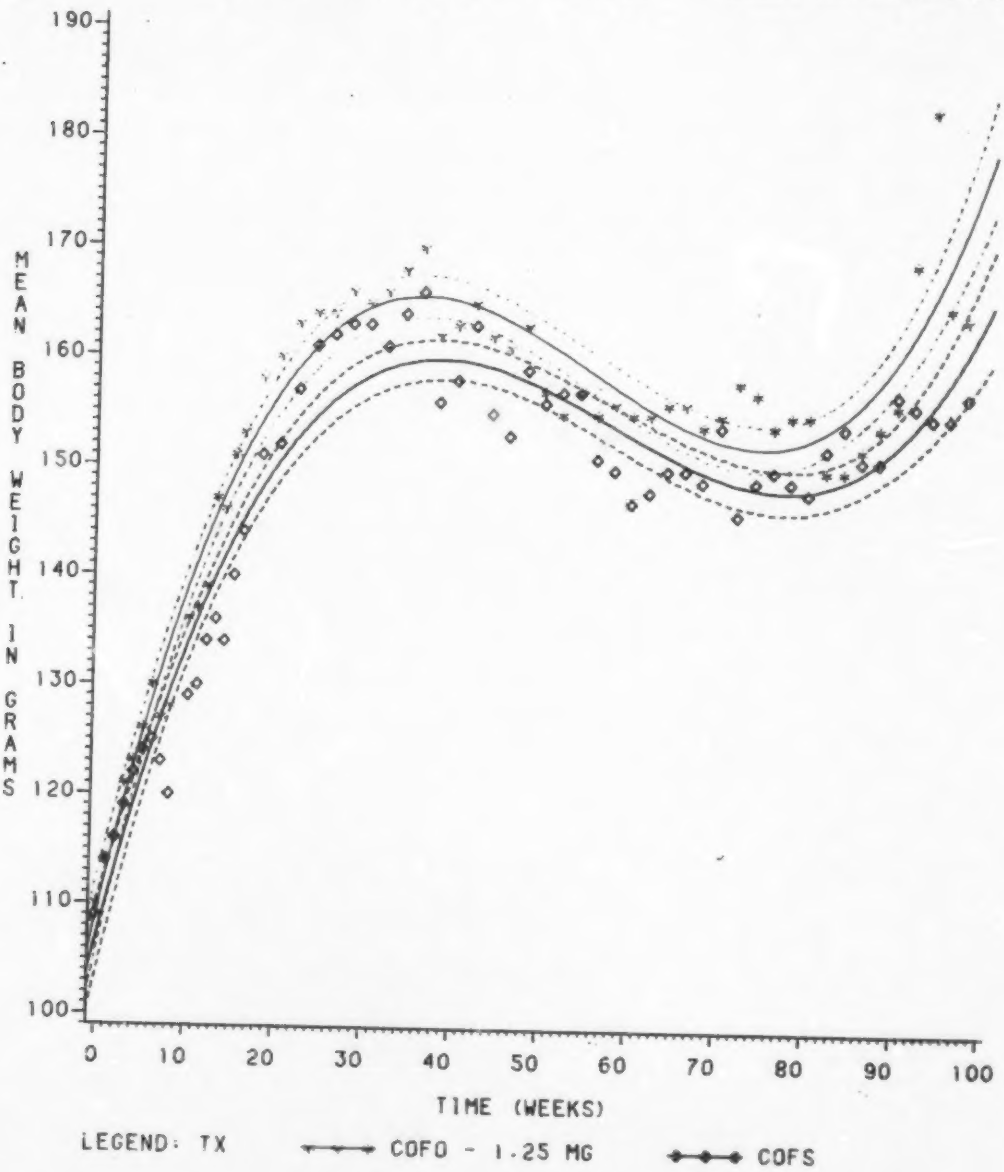
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND COFO(MEDIUM DOSE) AND COFS
MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

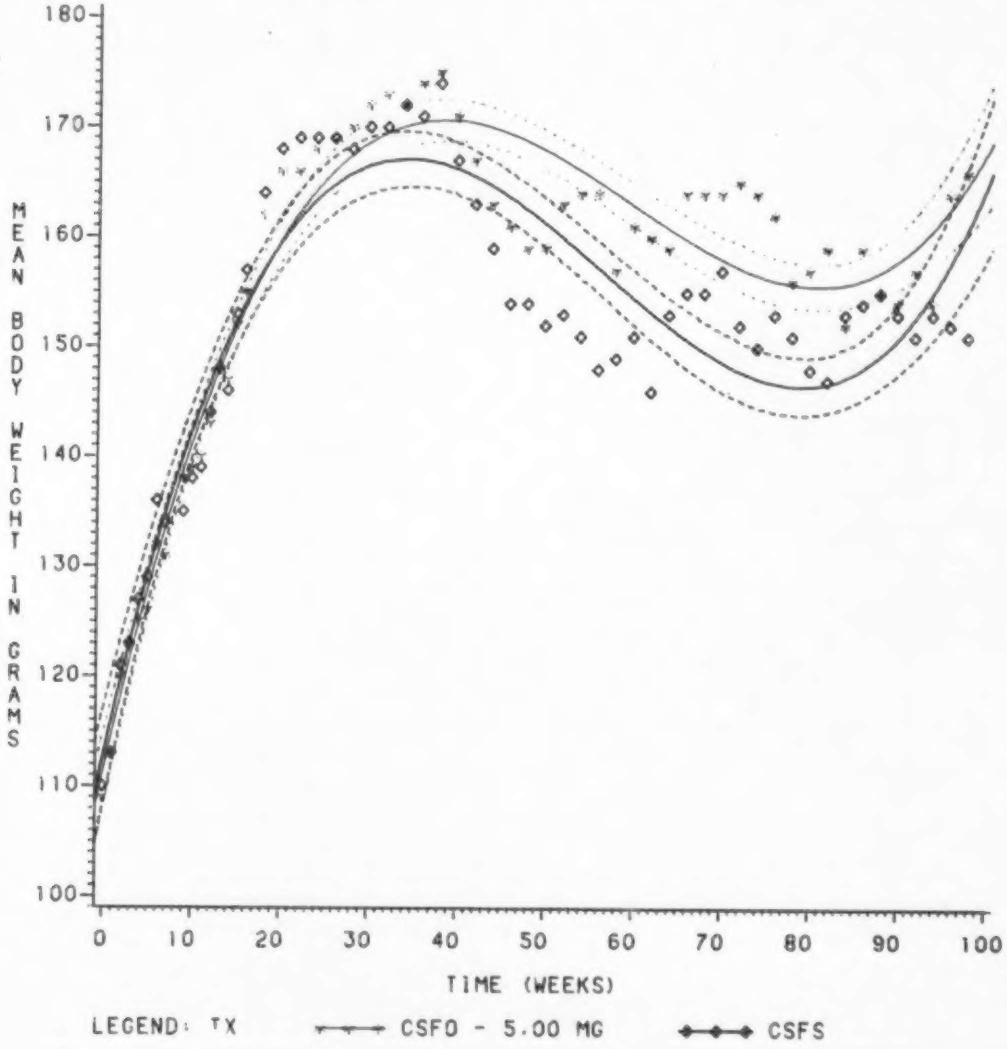
COMPOUND COFO(LOW DOSE) AND COFS
MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

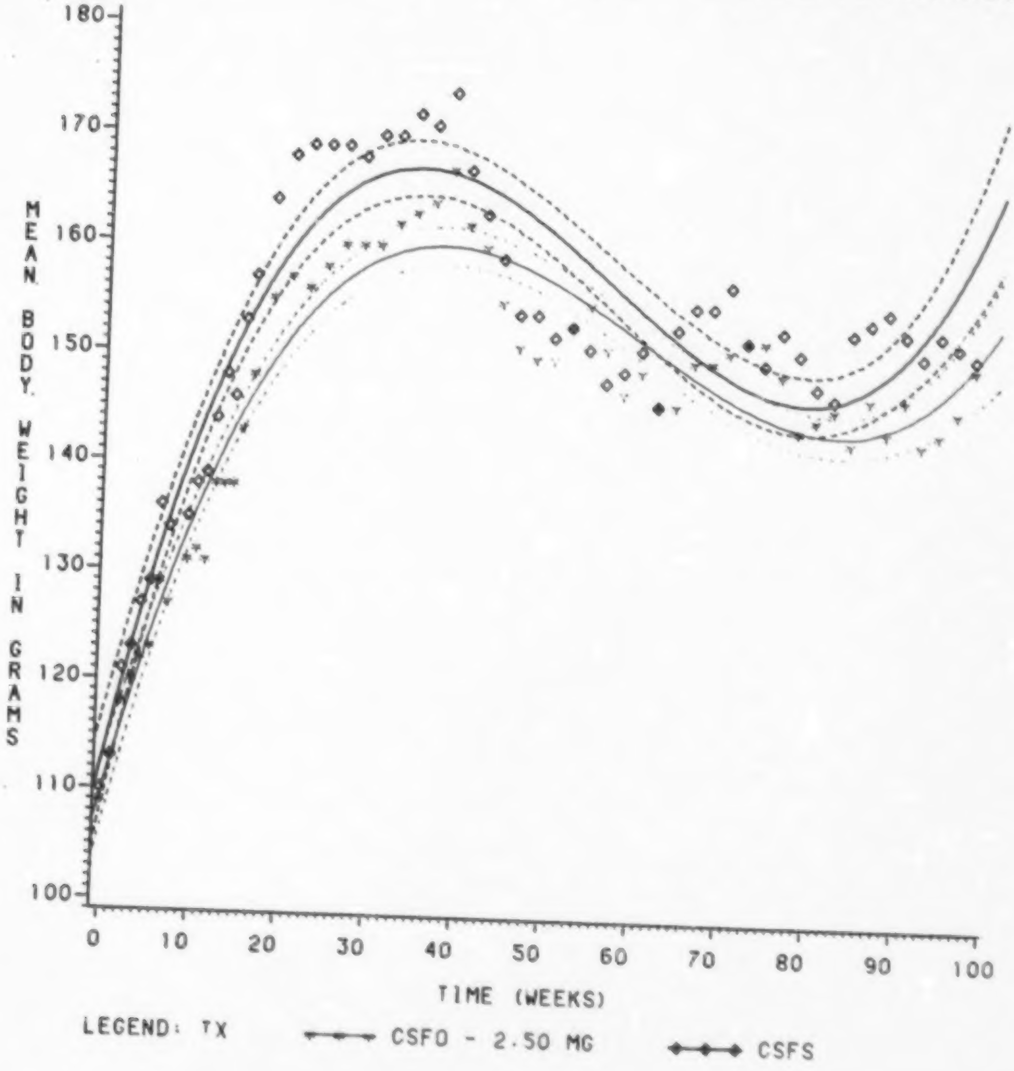
COMPOUND CSFO(HIGH DOSE) AND CSFS

MEAN BODY WEIGHT VS TIME - REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

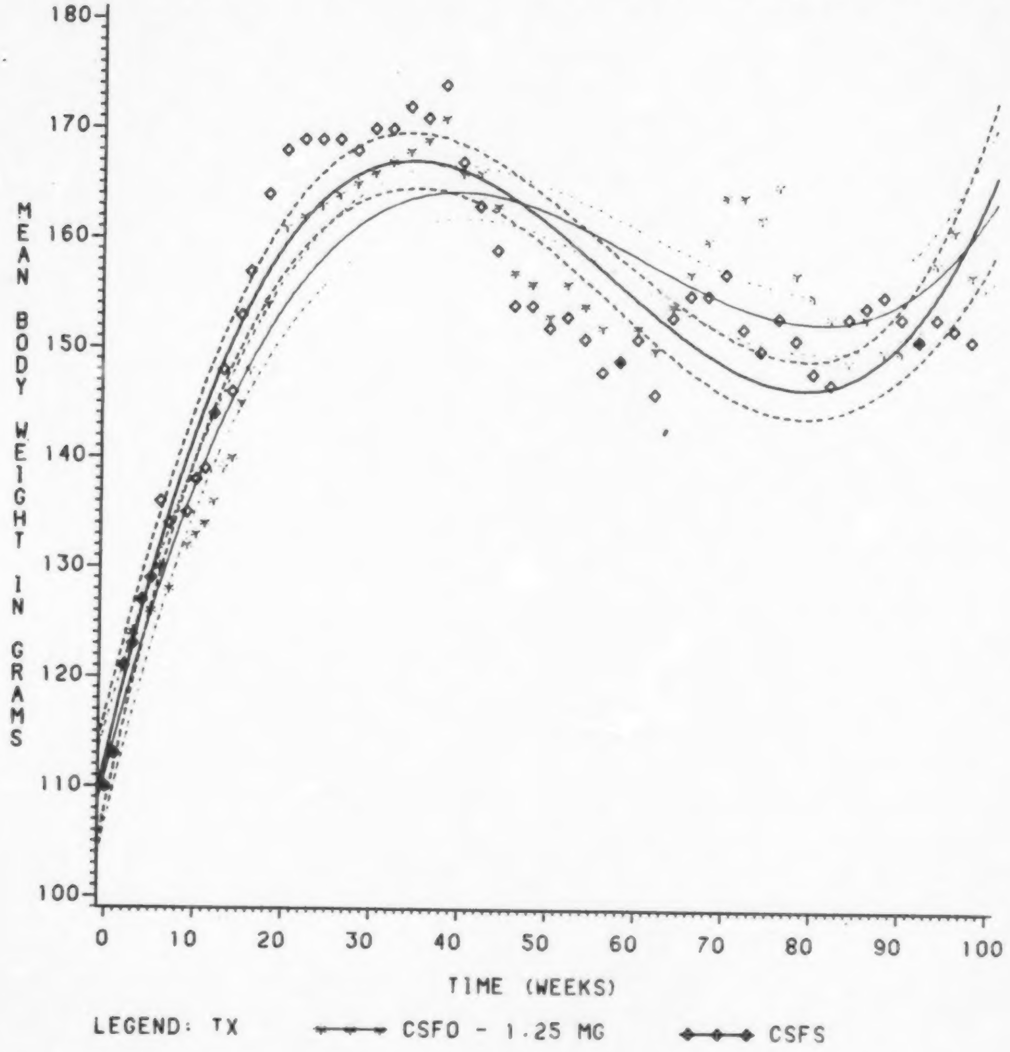
COMPOUND CSFO(MEDIUM DOSE) AND CSFS
MEAN BODY WEIGHT VS TIME - REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

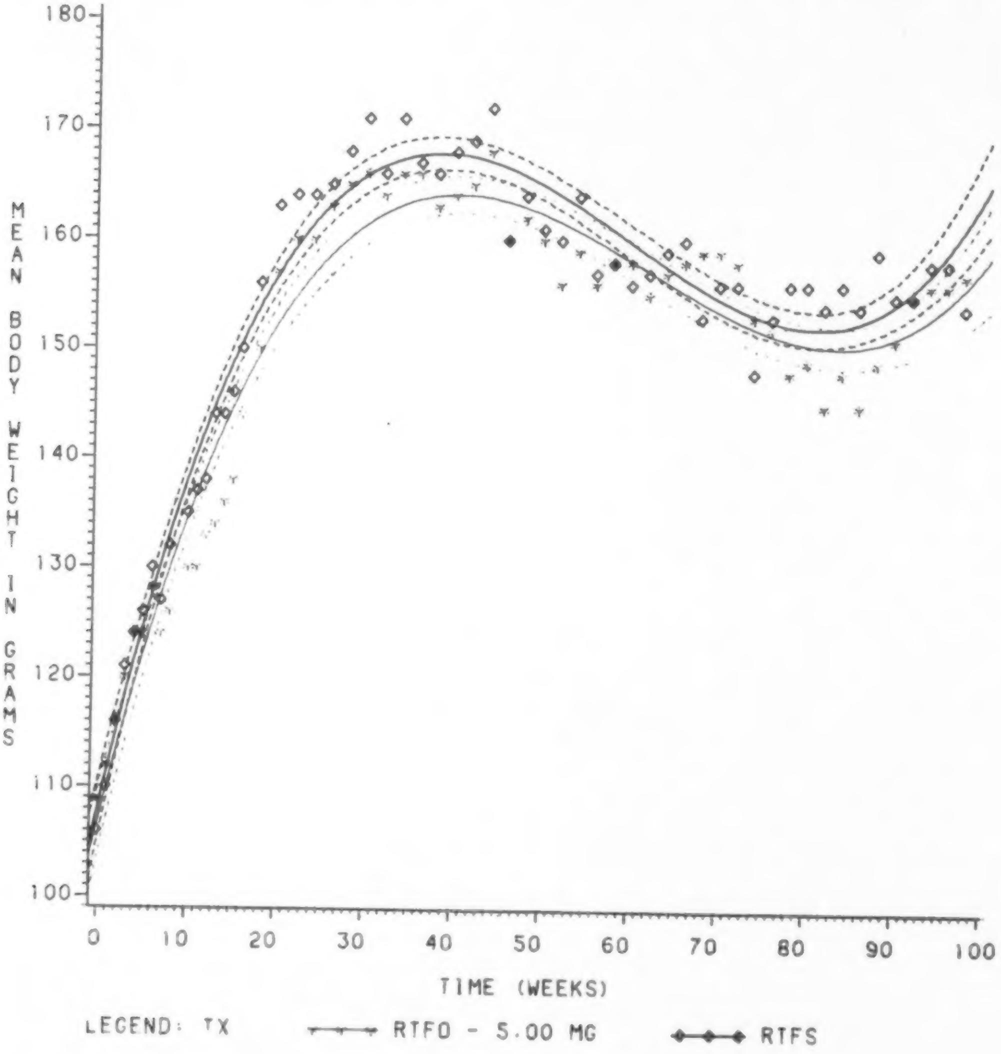
COMPOUND CSFO(LOW DOSE) AND CSFS

MEAN BODY WEIGHT VS TIME - REPLICATION 2



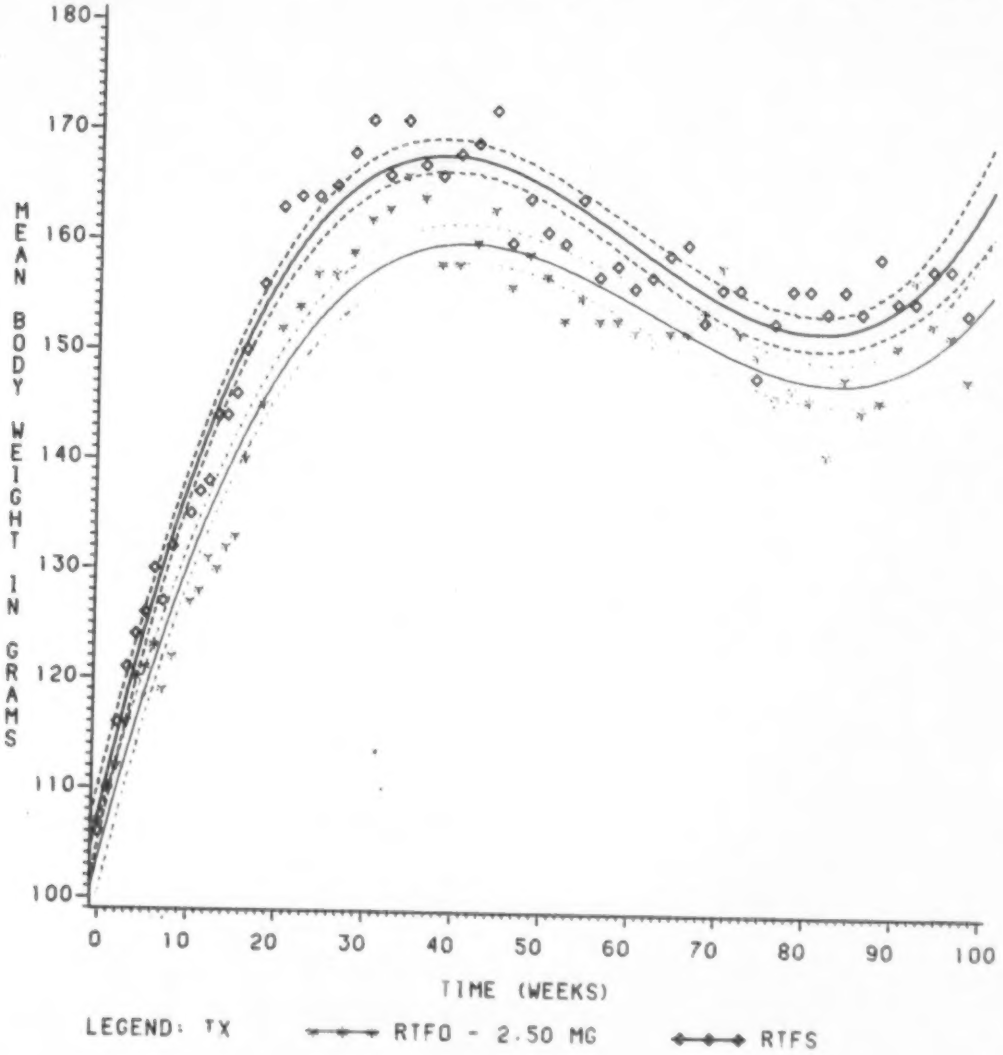
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND RTFO(HIGH DOSE) AND RTFS
MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

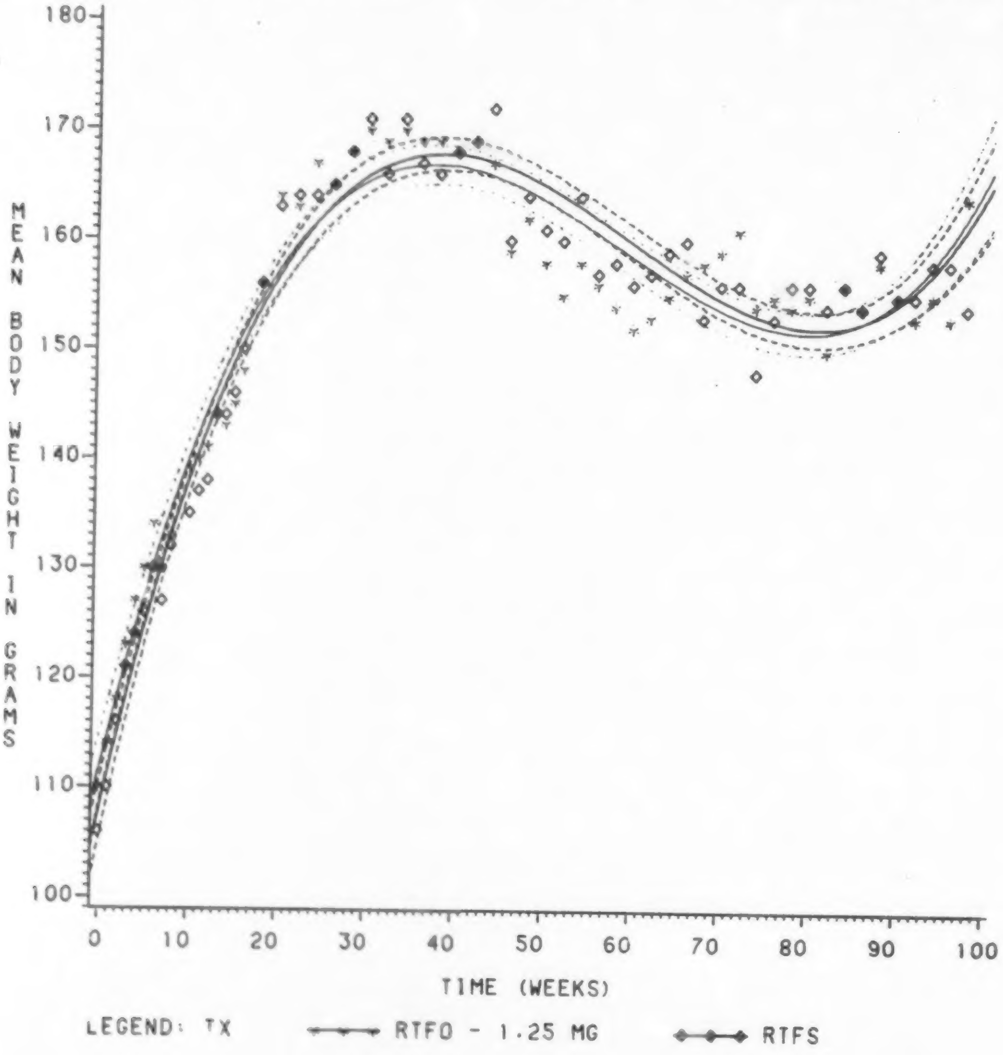
COMPOUND RTFO(MEDIUM DOSE) AND RTFS
MEAN BODY WEIGHT VS TIME - REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND RTFO(LOW DOSE) AND RTFS

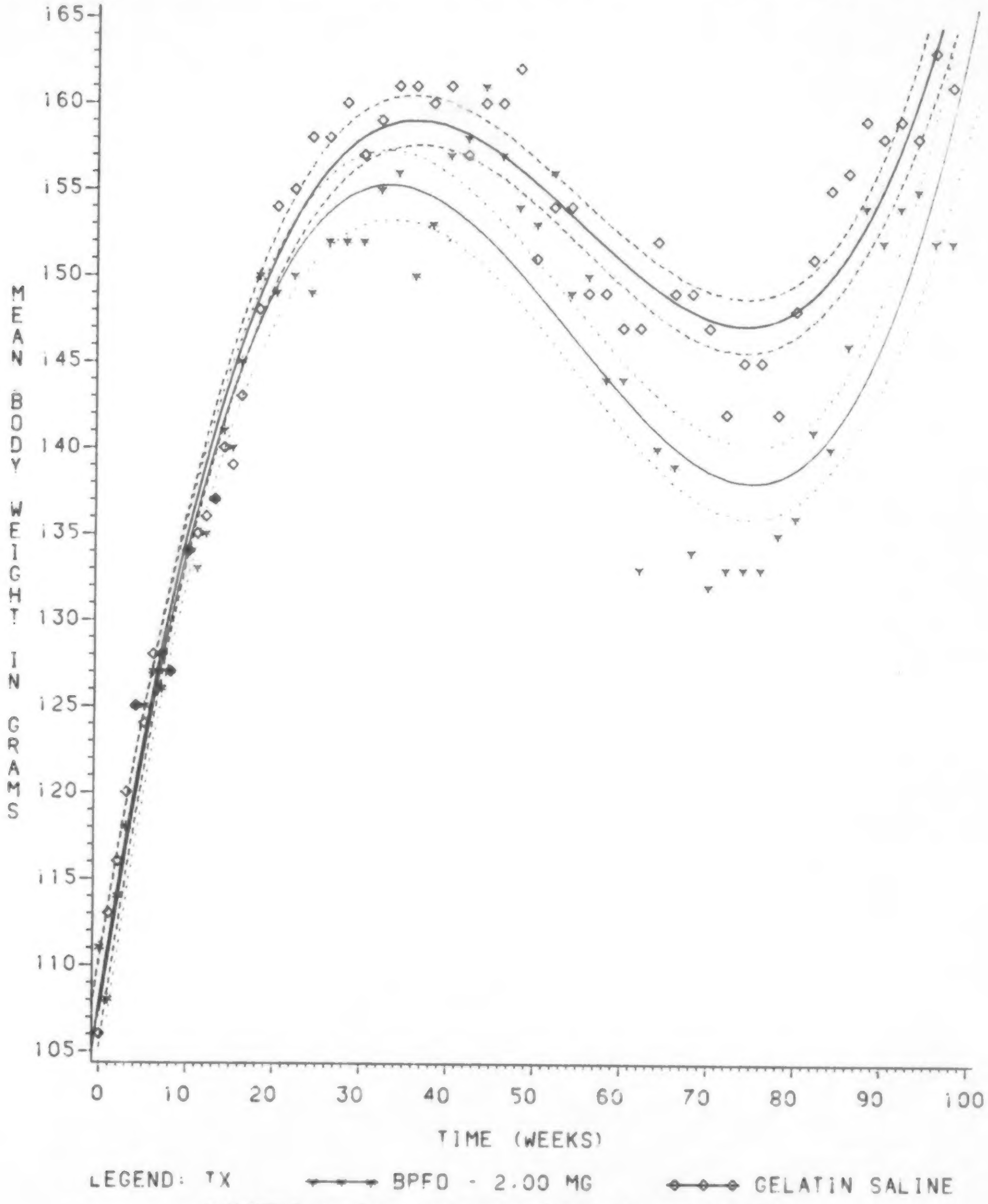
MEAN BODY WEIGHT VS TIME - REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

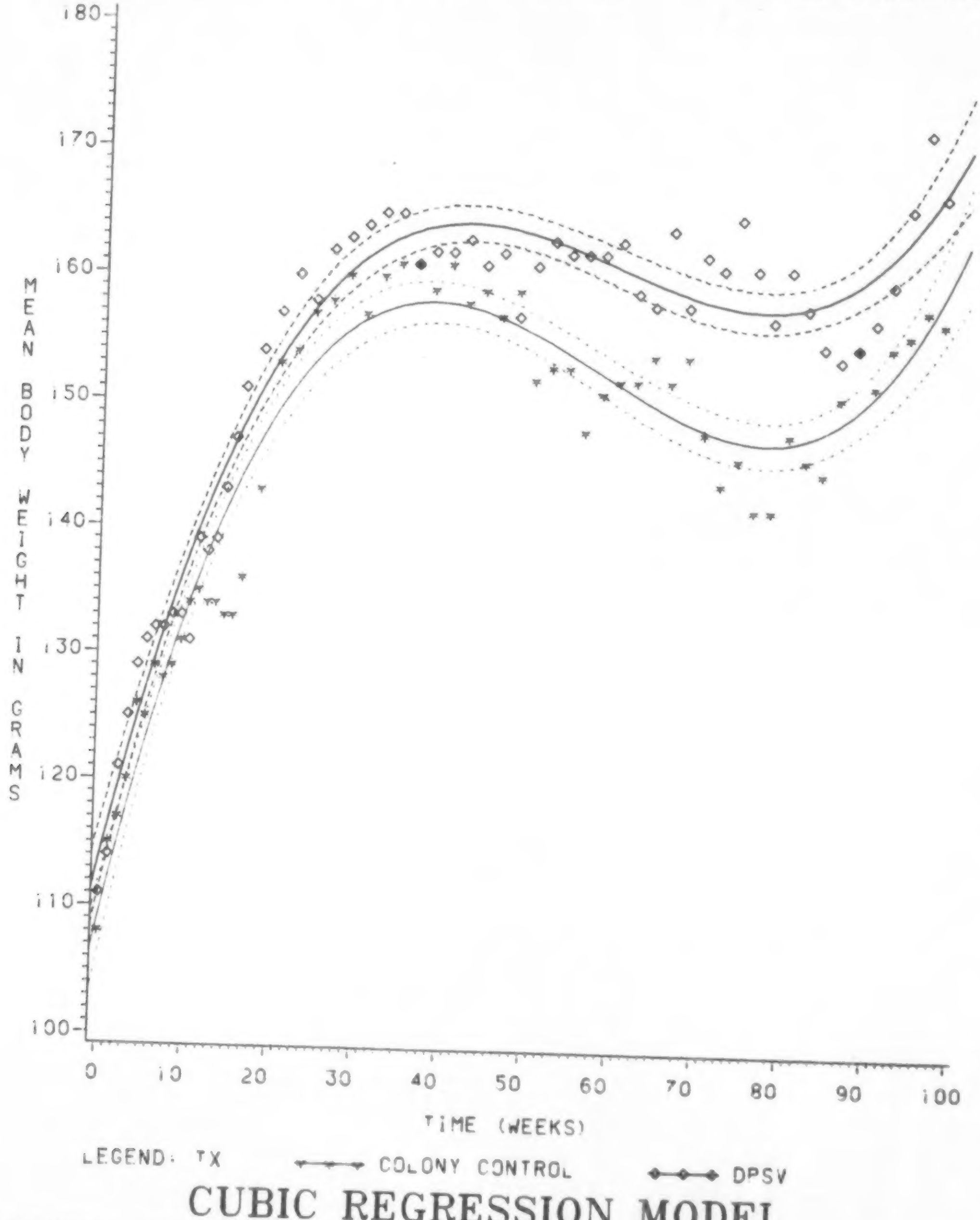
COMPOUND BPFO AND GELATIN SALINE

MEAN BODY WEIGHT VS TIME – REPLICATION 2



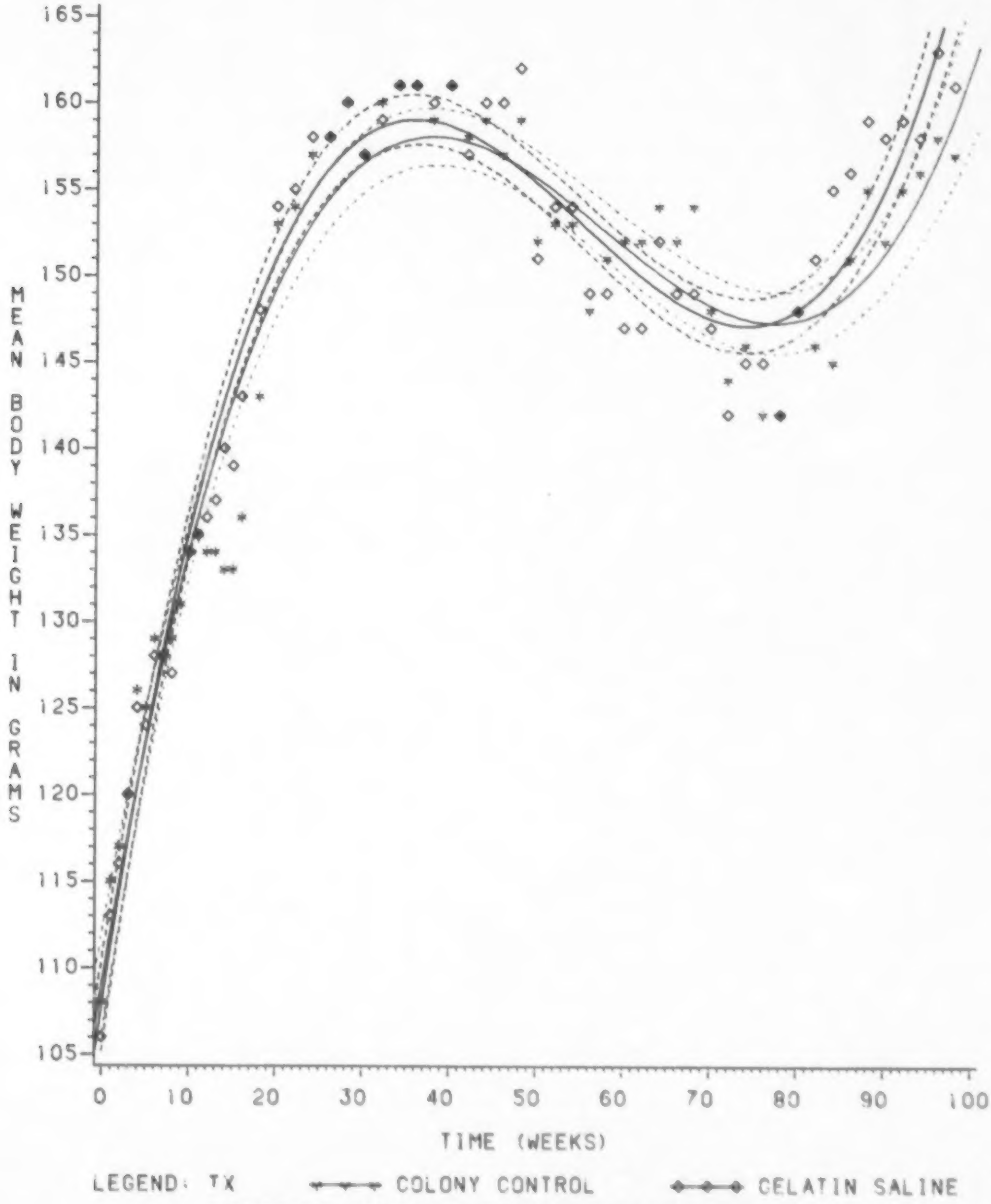
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

COMPOUND DPSV AND COLONY CONTROL
MEAN BODY WEIGHT VS TIME – REPLICATION 2



CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

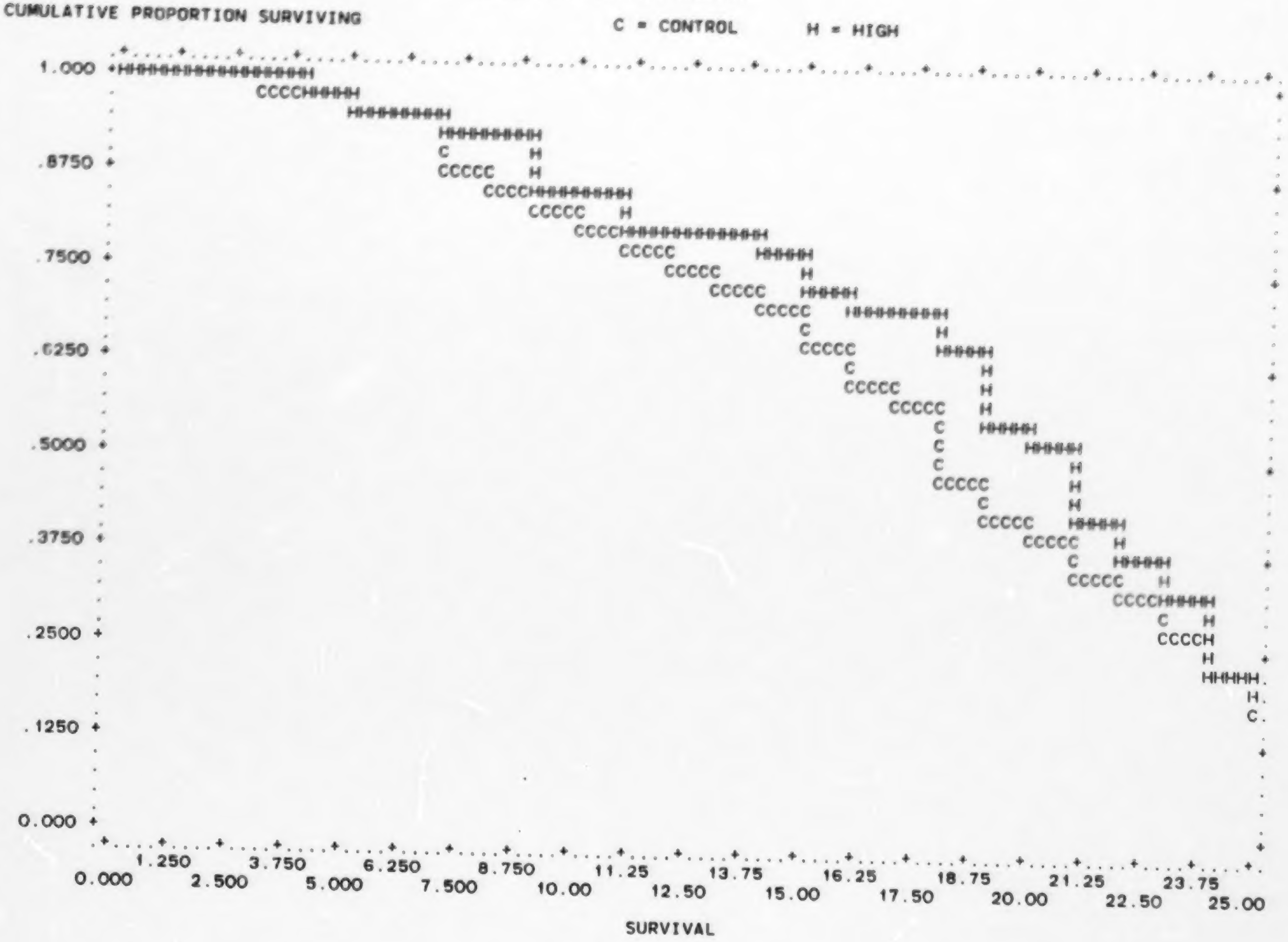
COMPOUND GELATIN SALINE AND COLONY CONTROL
MEAN BODY WEIGHT VS TIME – REPLICATION 2



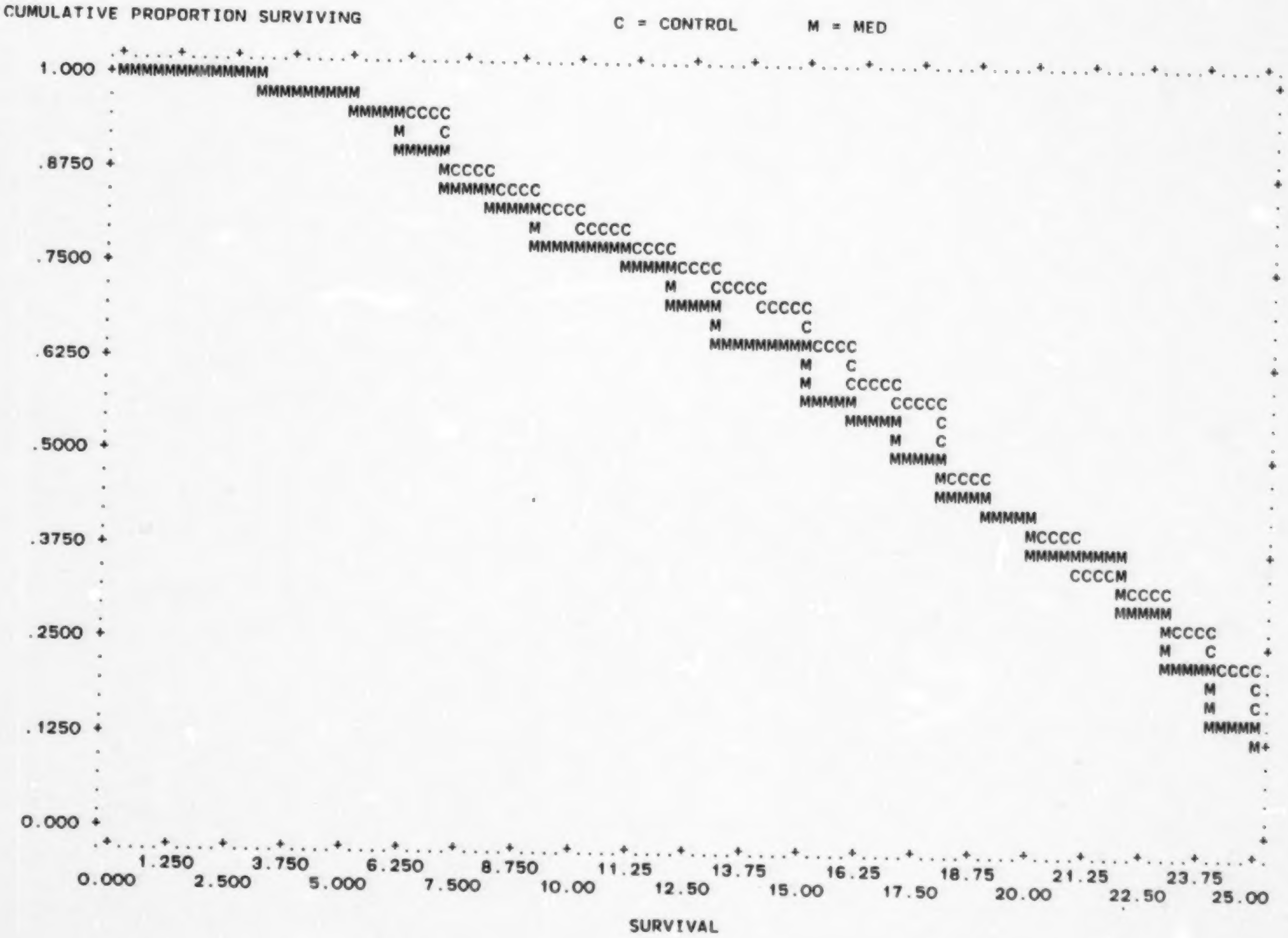
CUBIC REGRESSION MODEL
WITH 95 PERCENT CONFIDENCE INTERVALS

APPENDIX G
COMPUTER GENERATED SURVIVAL CURVES

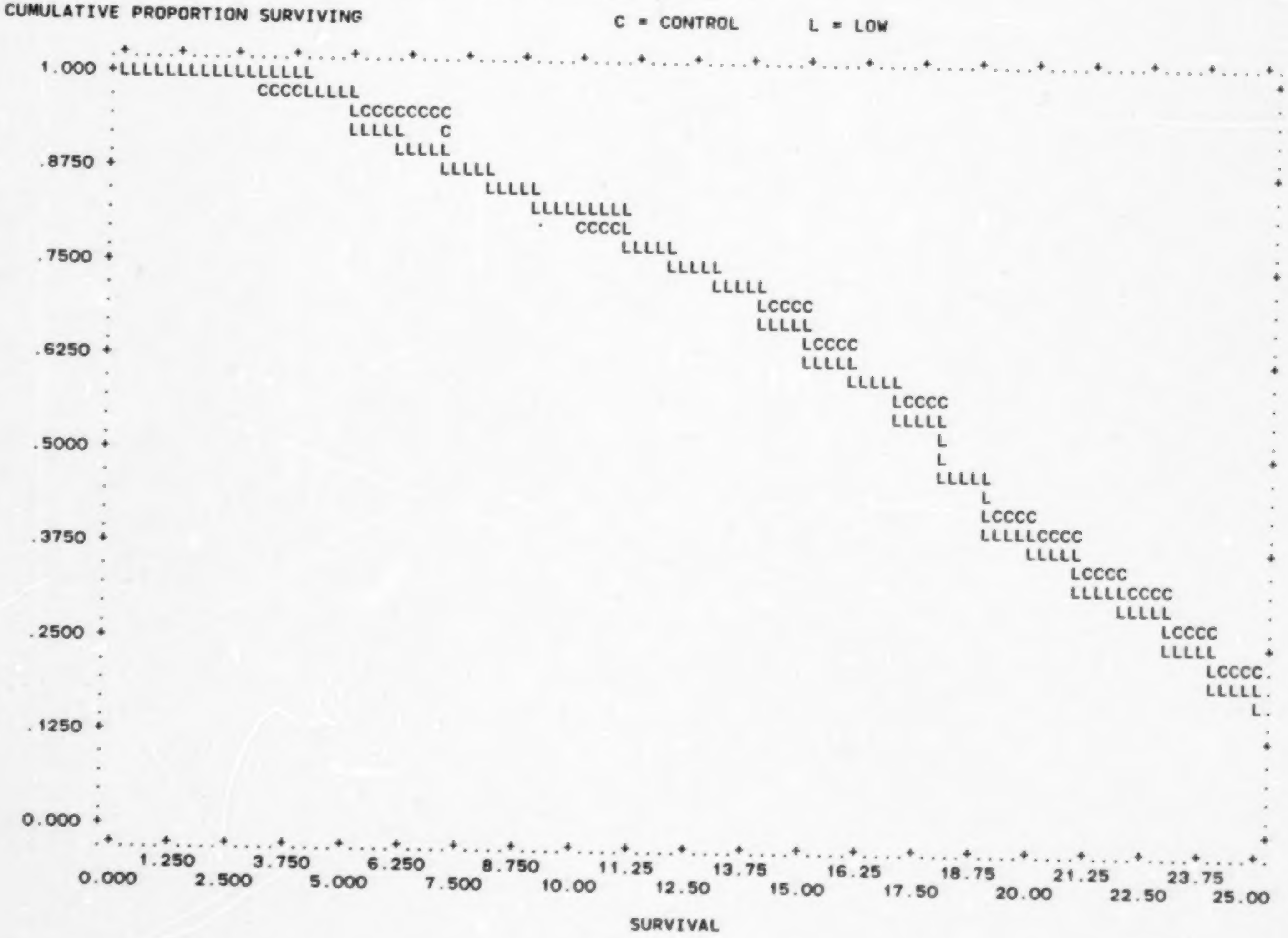
STUDY 6138 DPOO.DPSV - HIGH DOSE VS CONTROL ANALYSIS



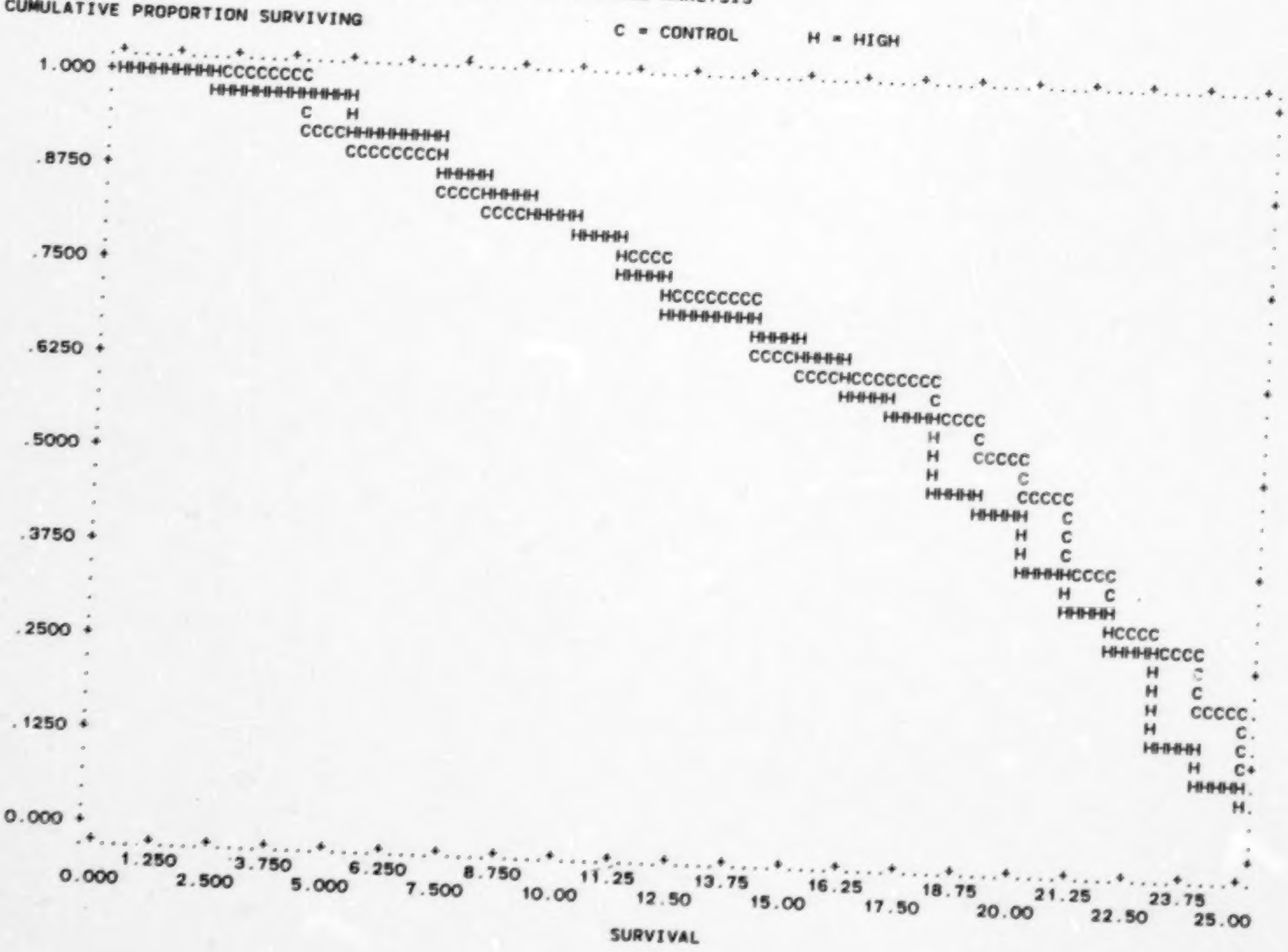
STUDY 6138 DPOO.DPSV - MED DOSE VS CONTROL ANALYSIS



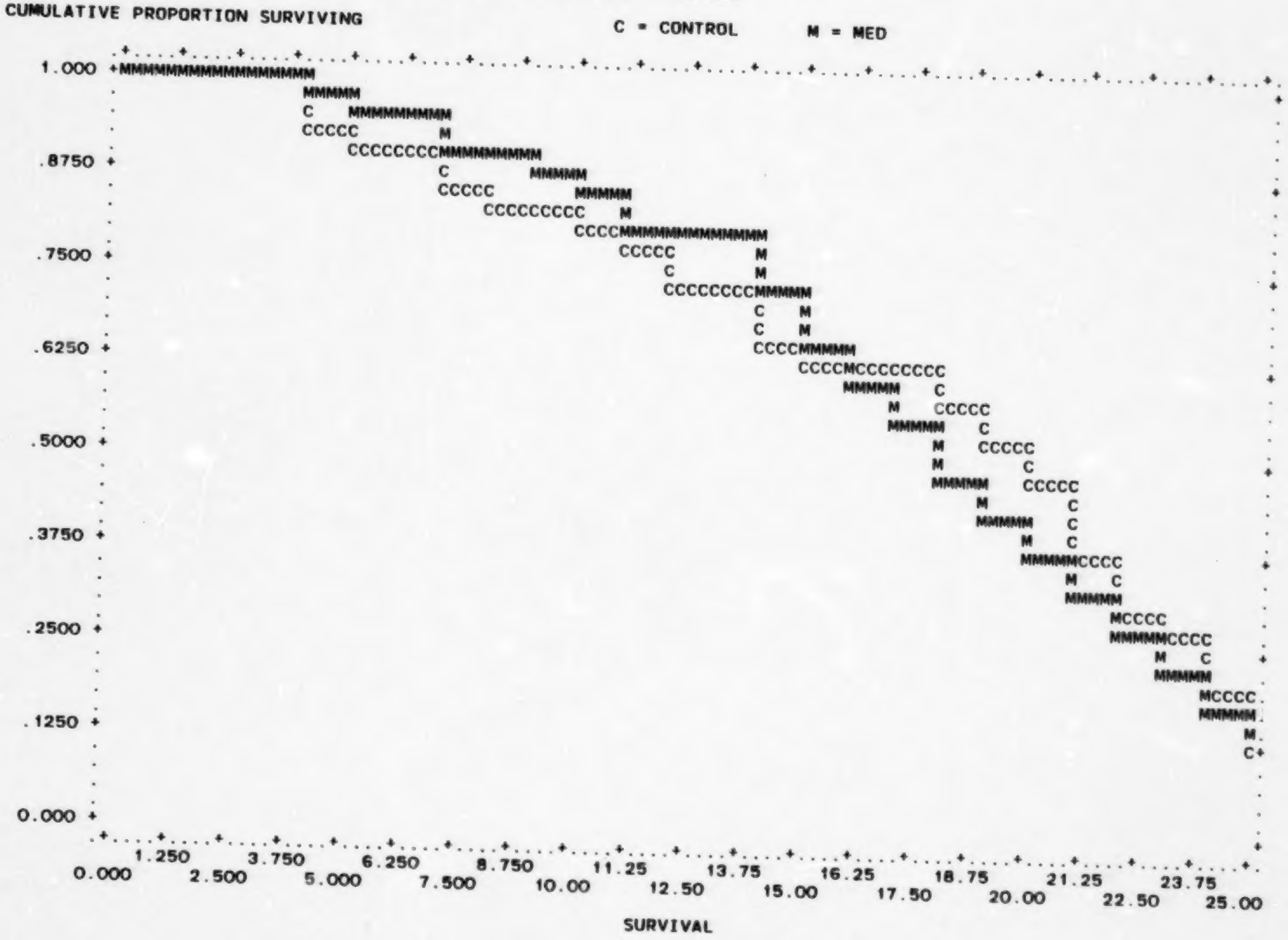
STUDY 6138 DPOO,DPSV - LOW DOSE VS CONTROL ANALYSIS



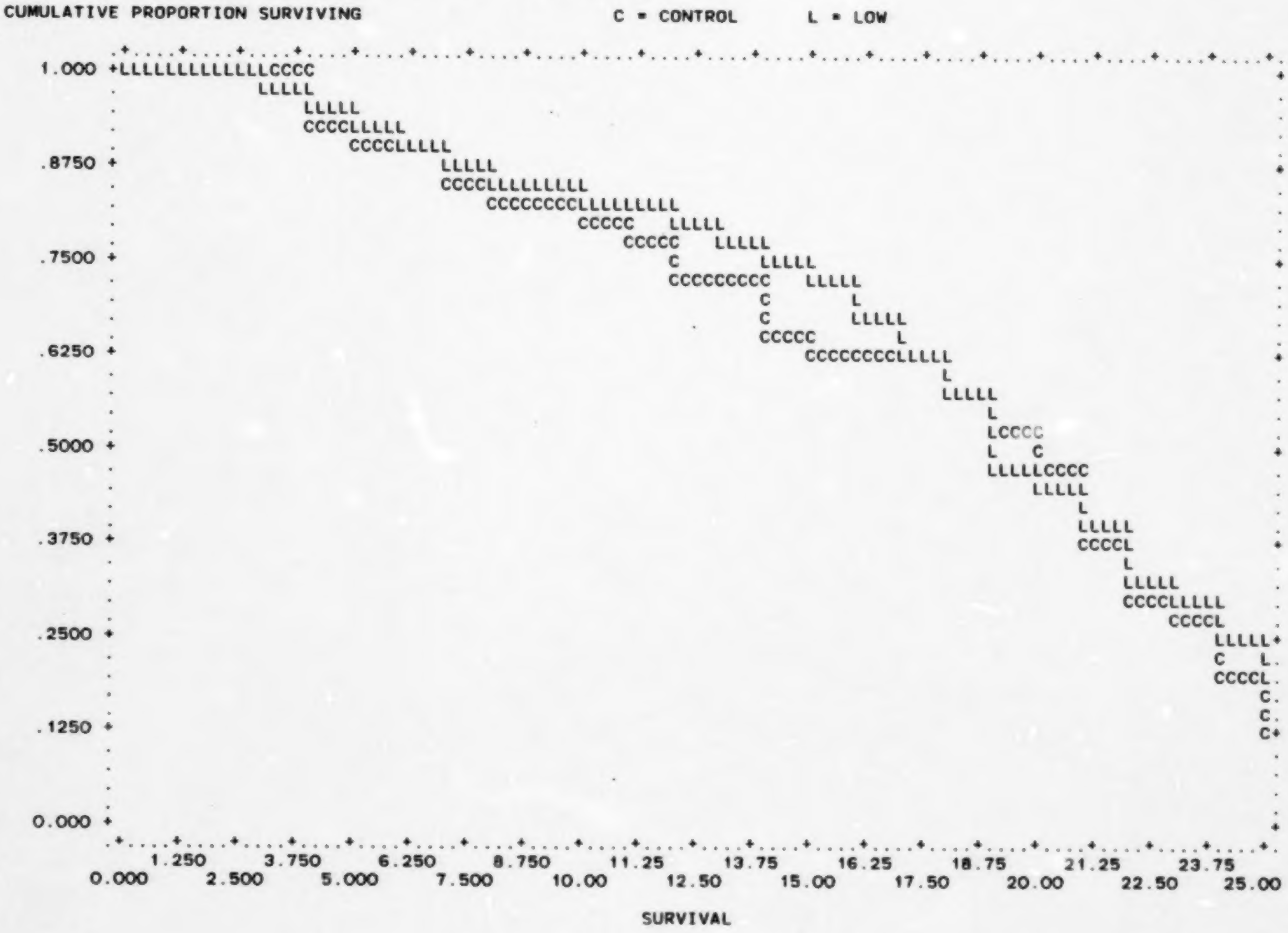
STUDY 6138 DPFO.DPFS - HIGH DOSE VS CONTROL ANALYSIS



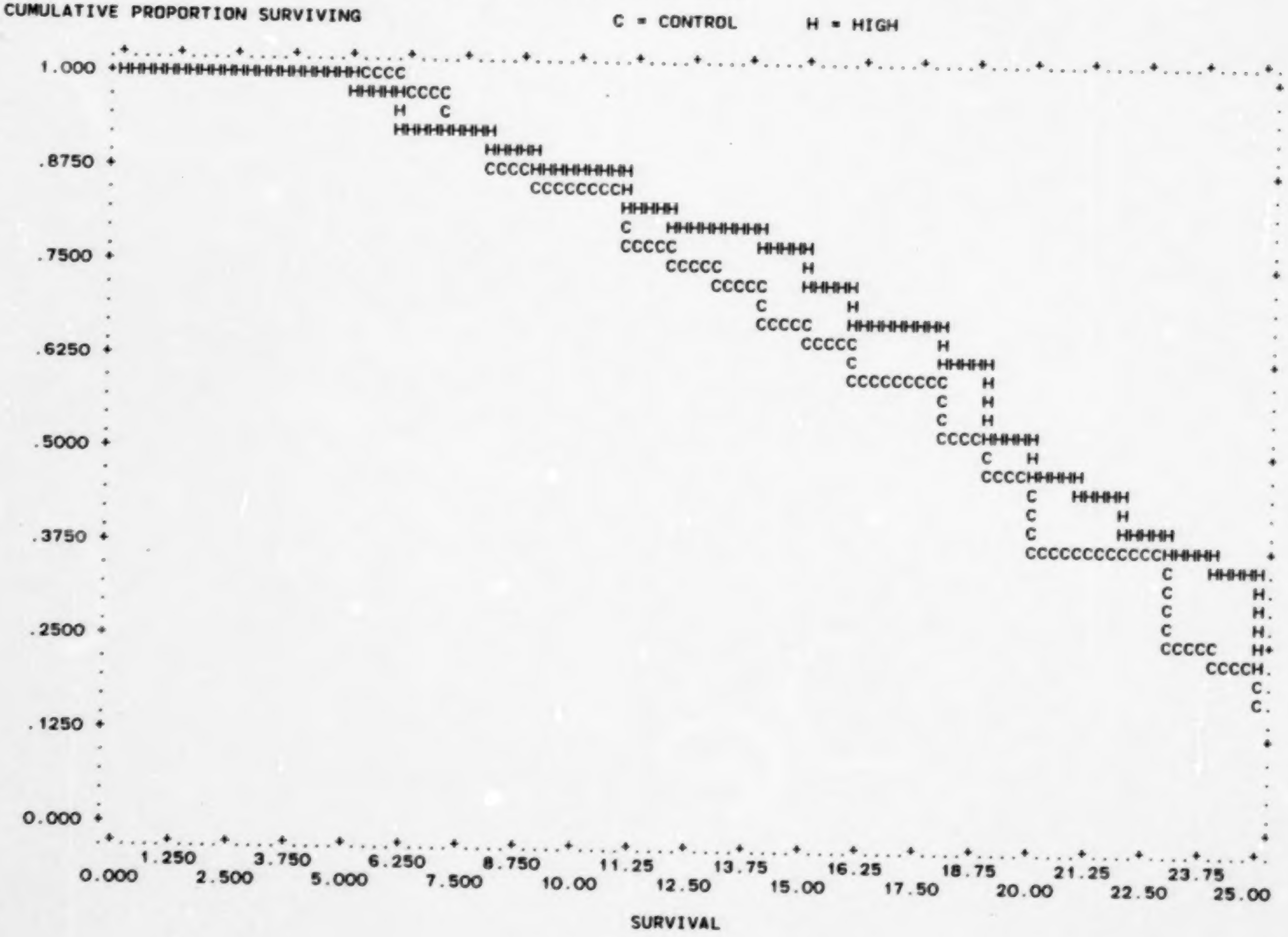
STUDY 6138 DPFO.DPFS - MED DOSE VS CONTROL ANALYSIS



STUDY 6138 DPFO,DPFS - LOW DOSE VS CONTROL ANALYSIS



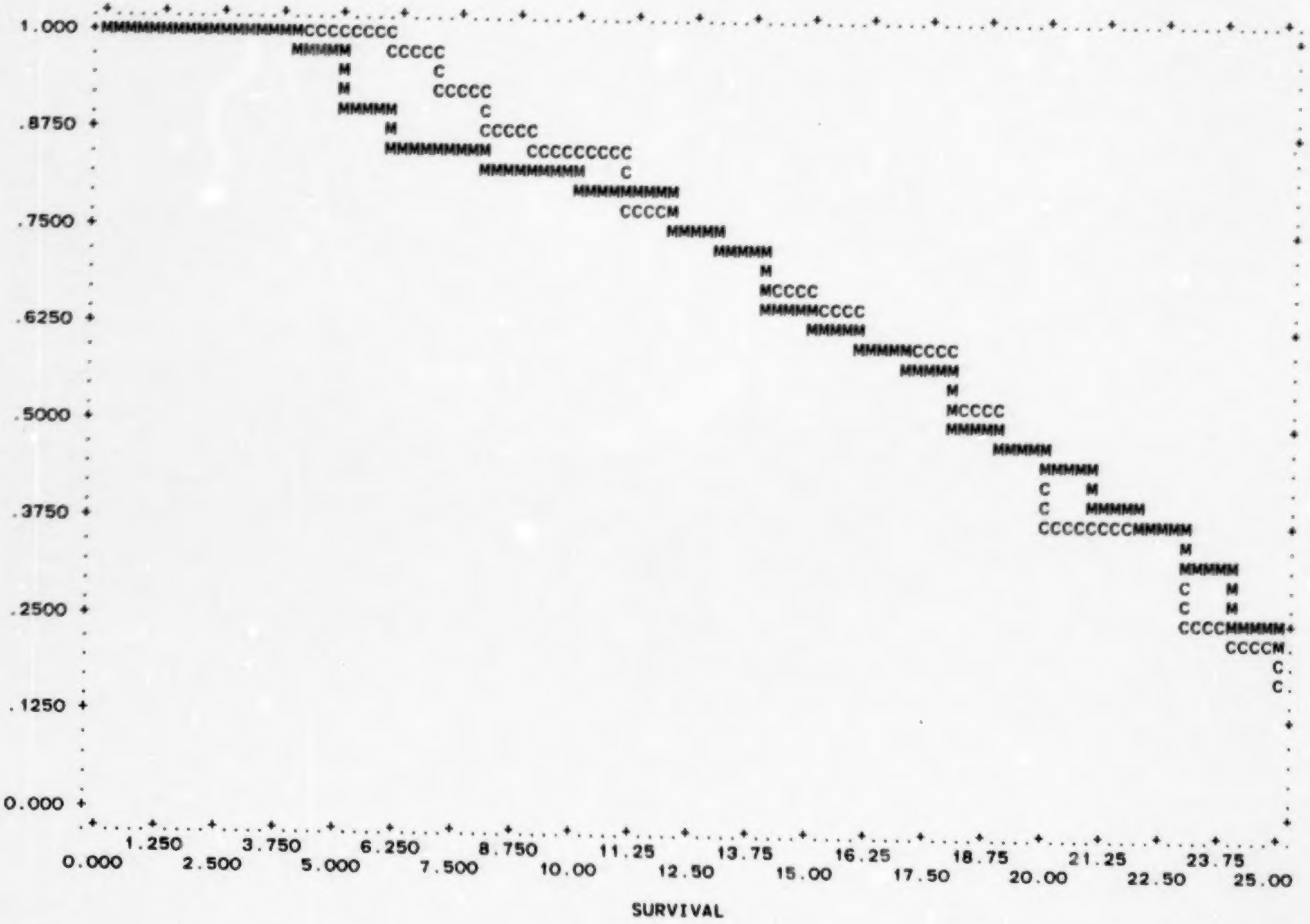
STUDY 6138 DEFO.DEFS - HIGH DOSE VS CONTROL ANALYSIS



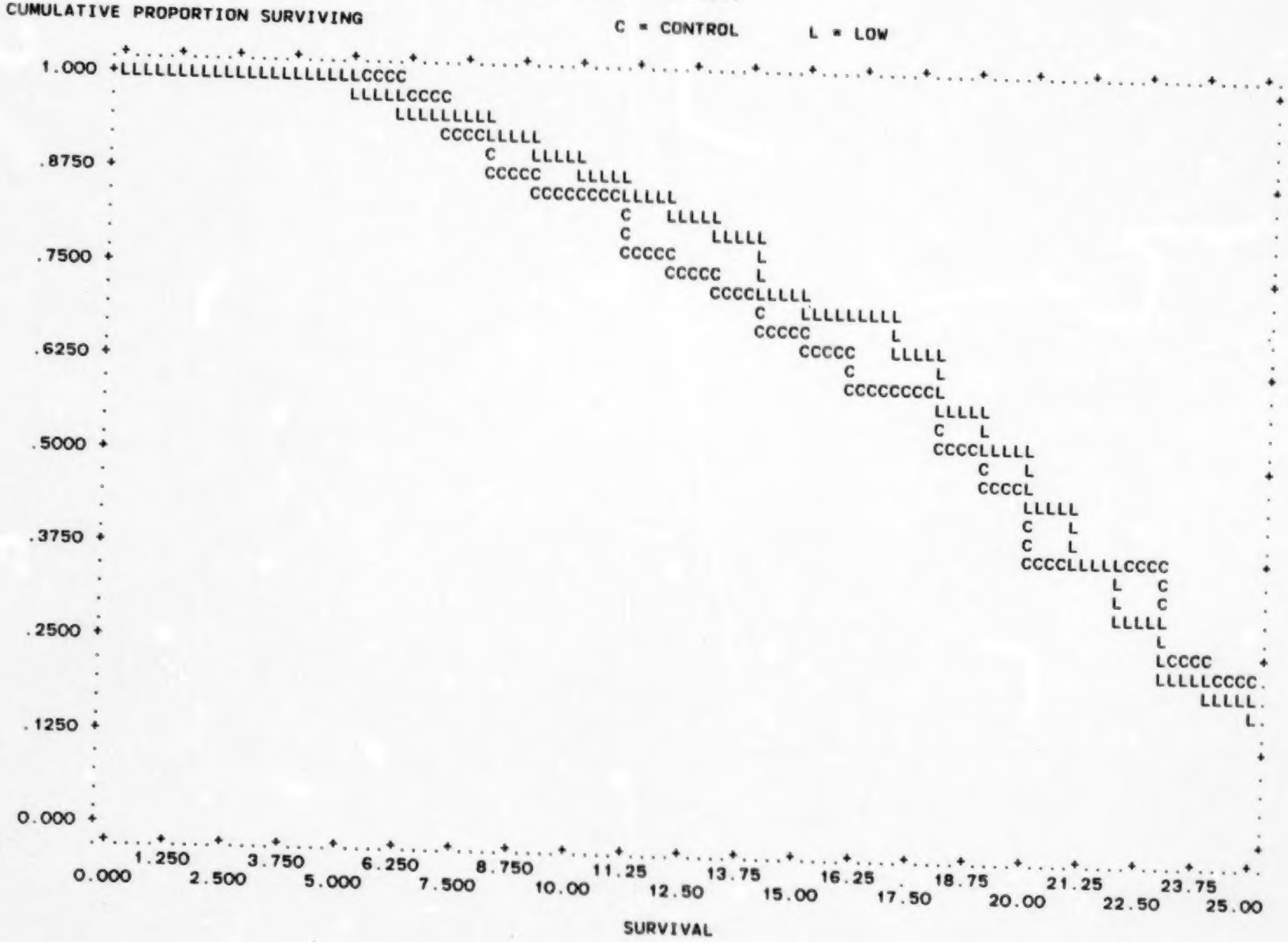
STUDY 6138 DEFO,DEFS - MED DOSE VS CONTROL ANALYSIS

CUMULATIVE PROPORTION SURVIVING

C = CONTROL M = MED

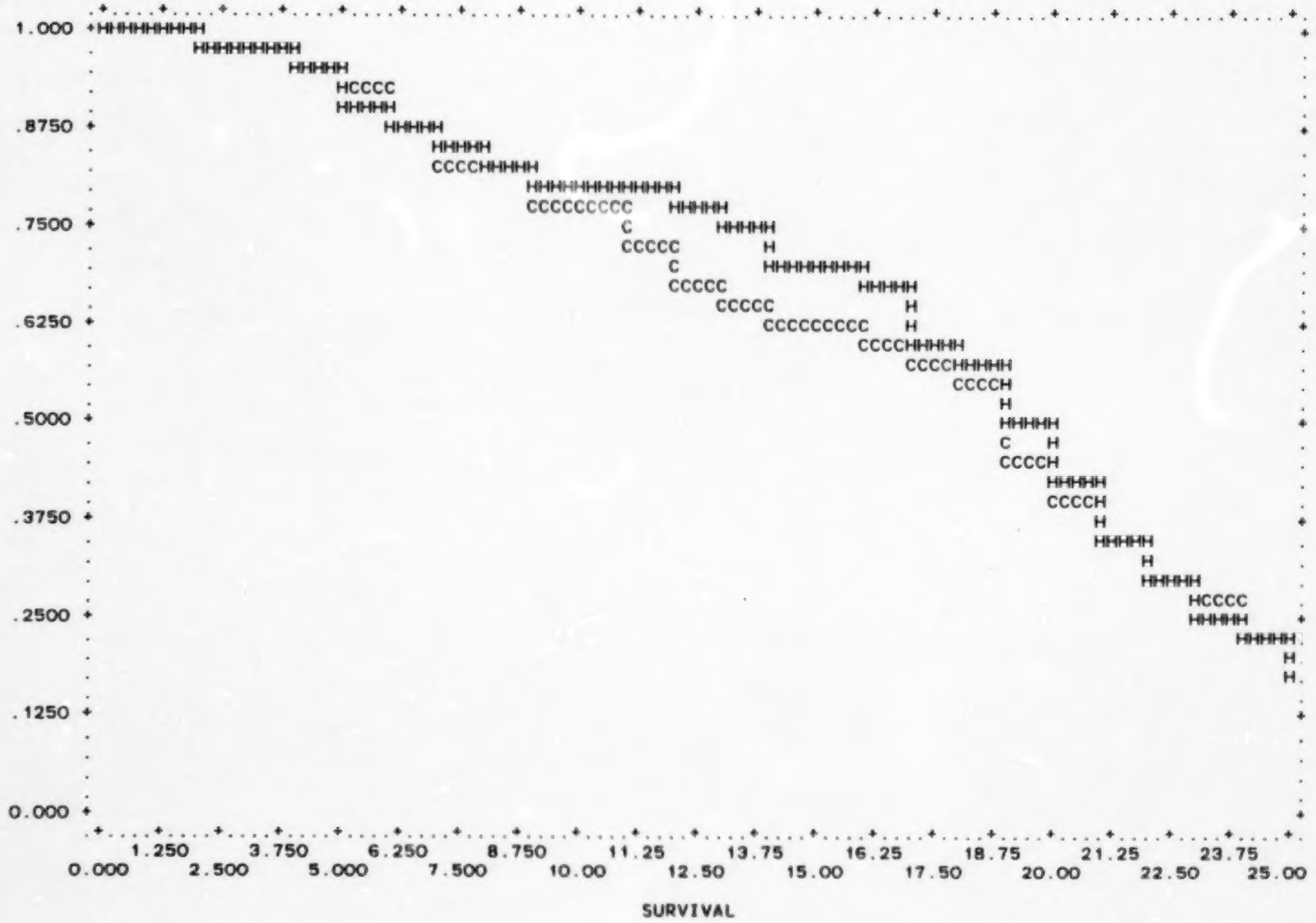


STUDY 6138 DEFO.DEFS - LOW DOSE VS CONTROL ANALYSIS

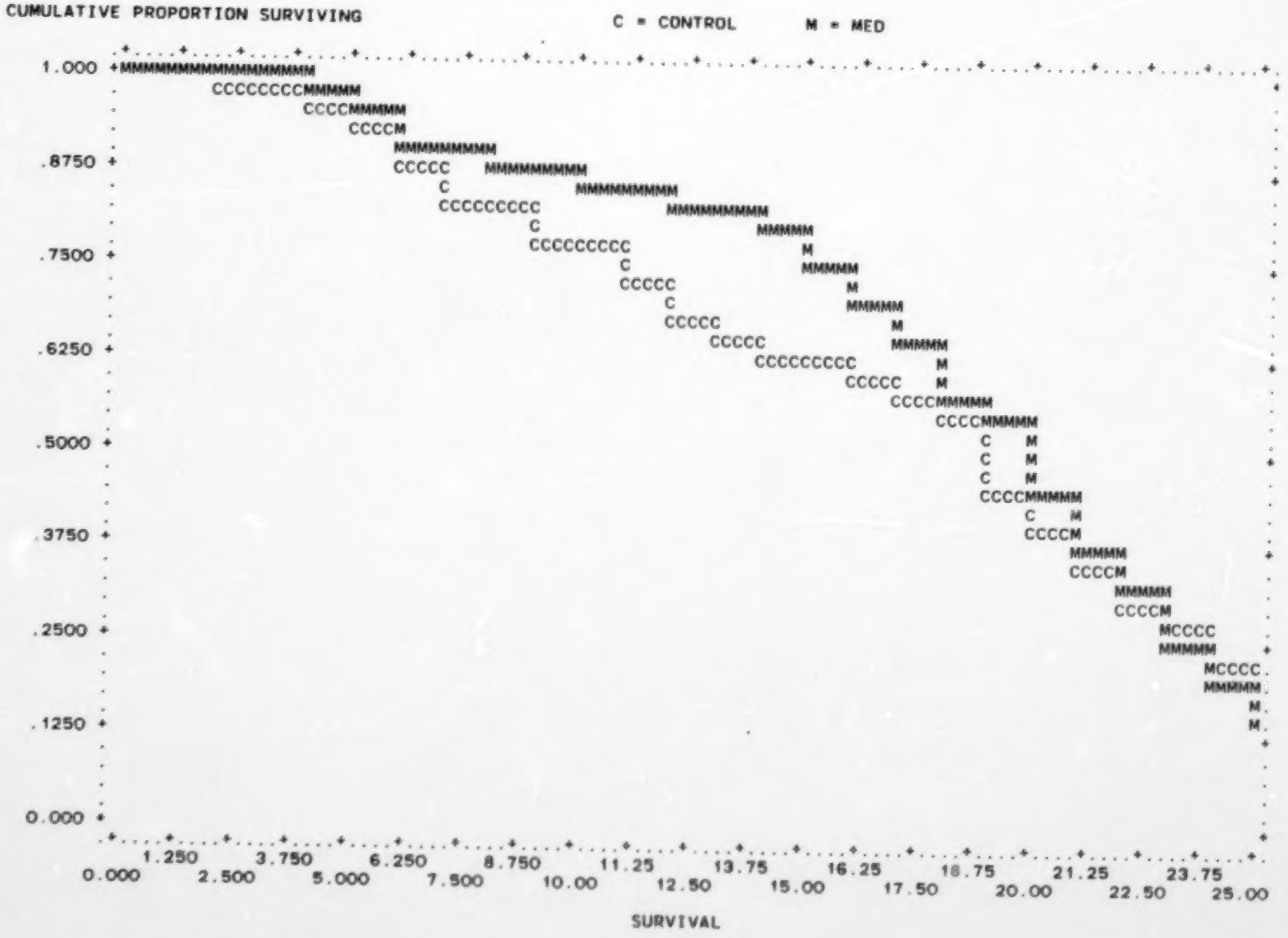


STUDY 6138 COFO.COFS - HIGH DOSE VS CONTROL ANALYSIS

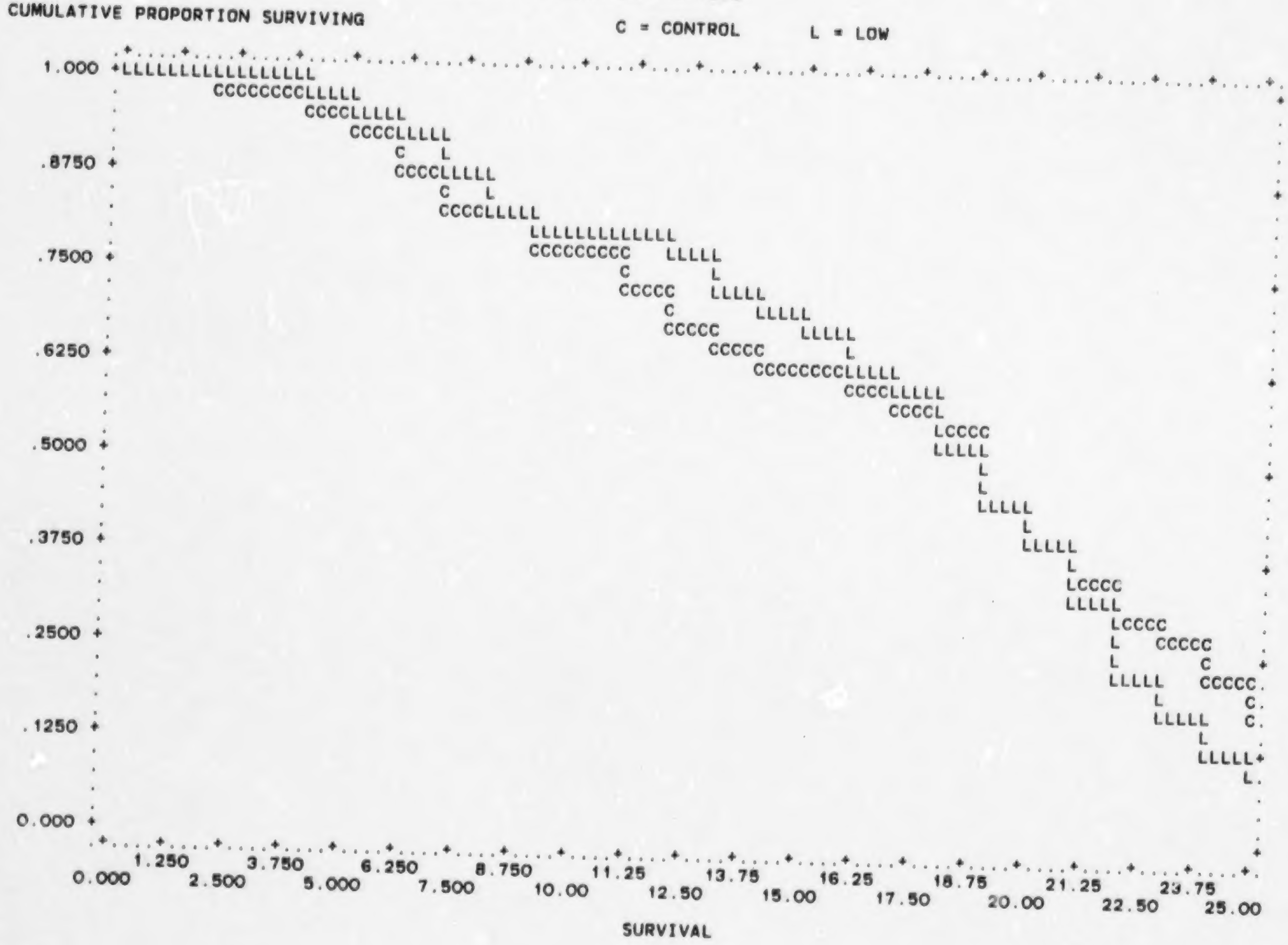
CUMULATIVE PROPORTION SURVIVING C = CONTROL H = HIGH



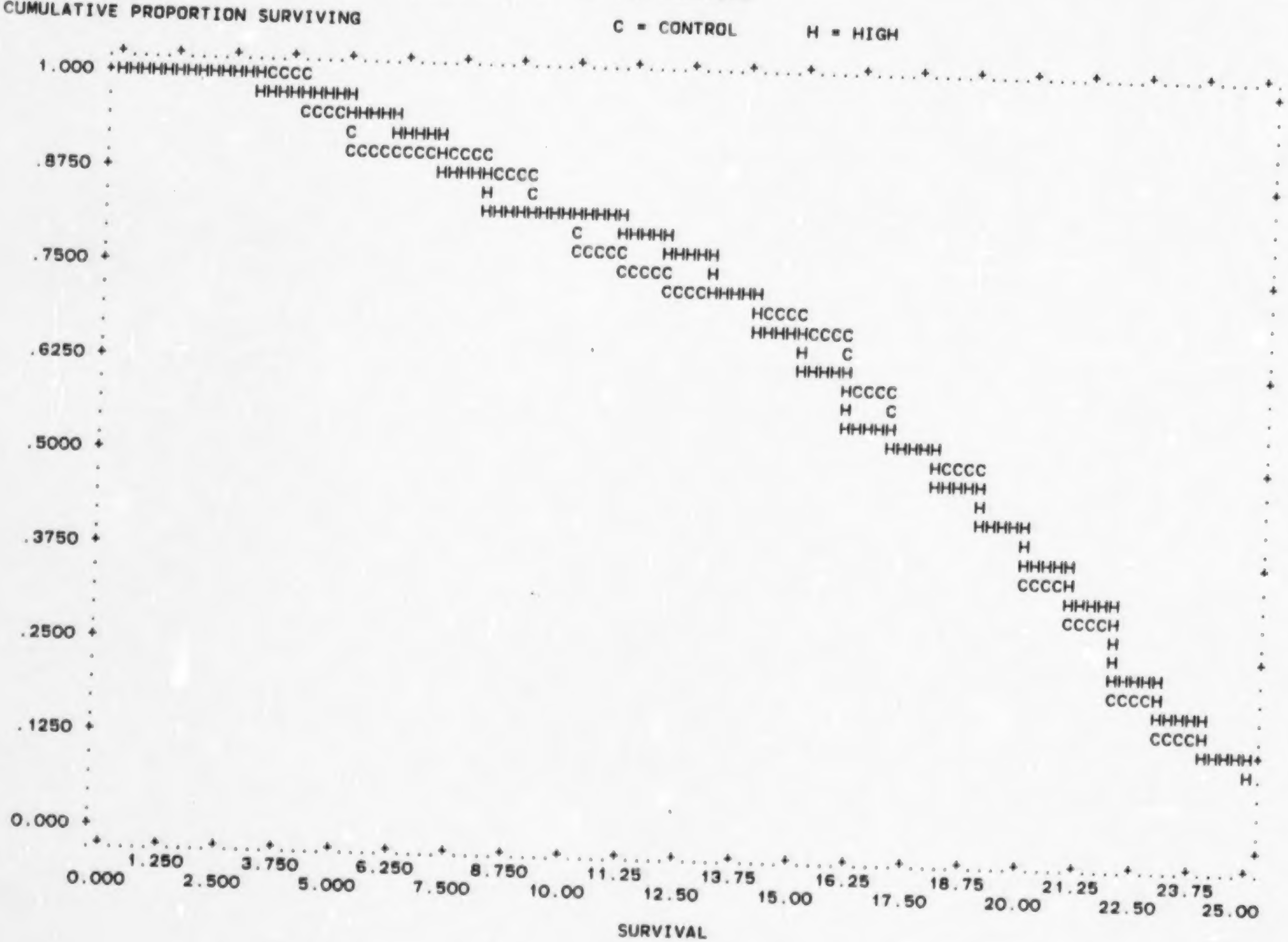
STUDY 6138 COFO.COFS - MED DOSE VS CONTROL ANALYSIS



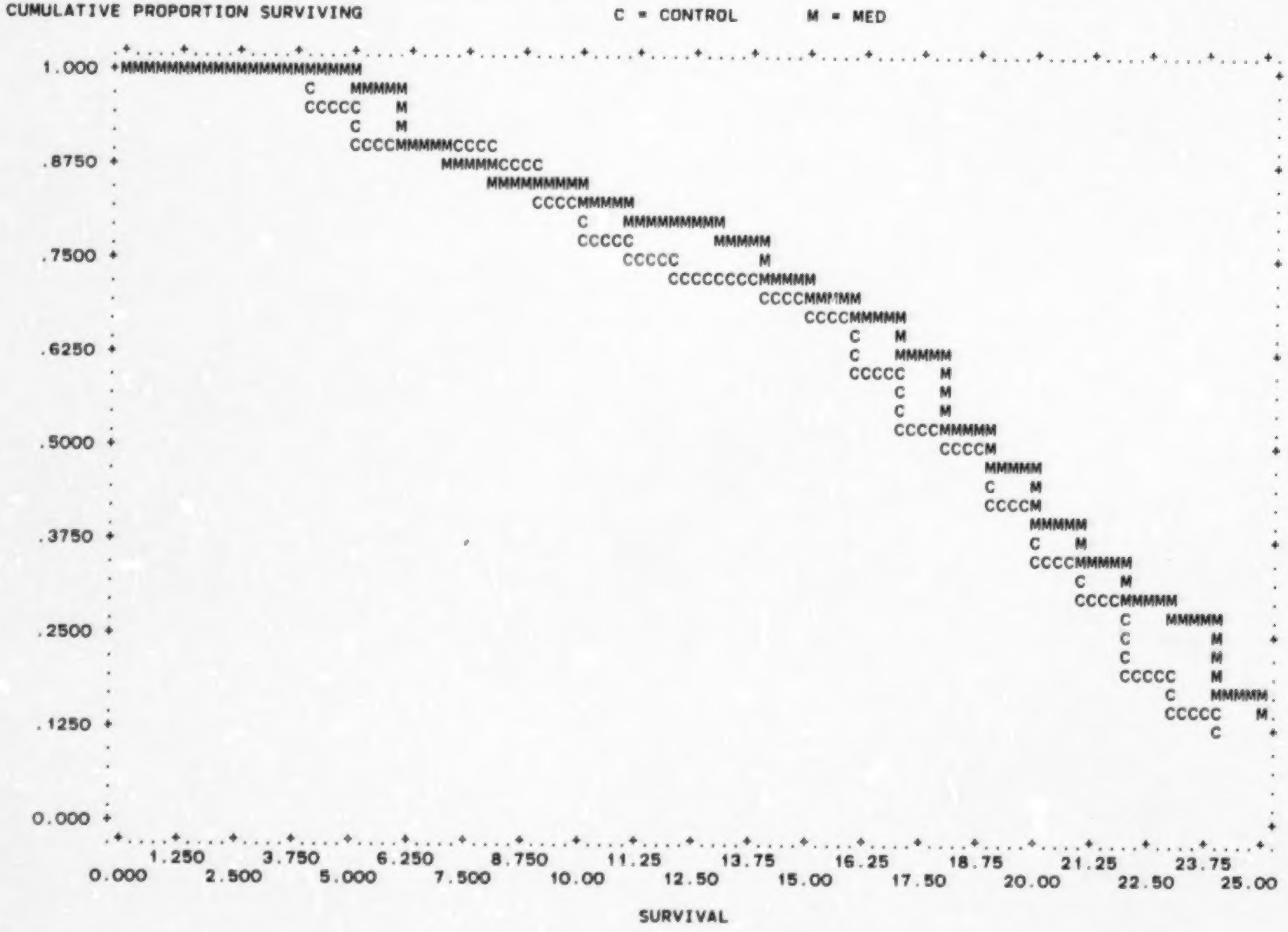
STUDY 6138 COFO.COFS - LOW DOSE VS CONTROL ANALYSIS



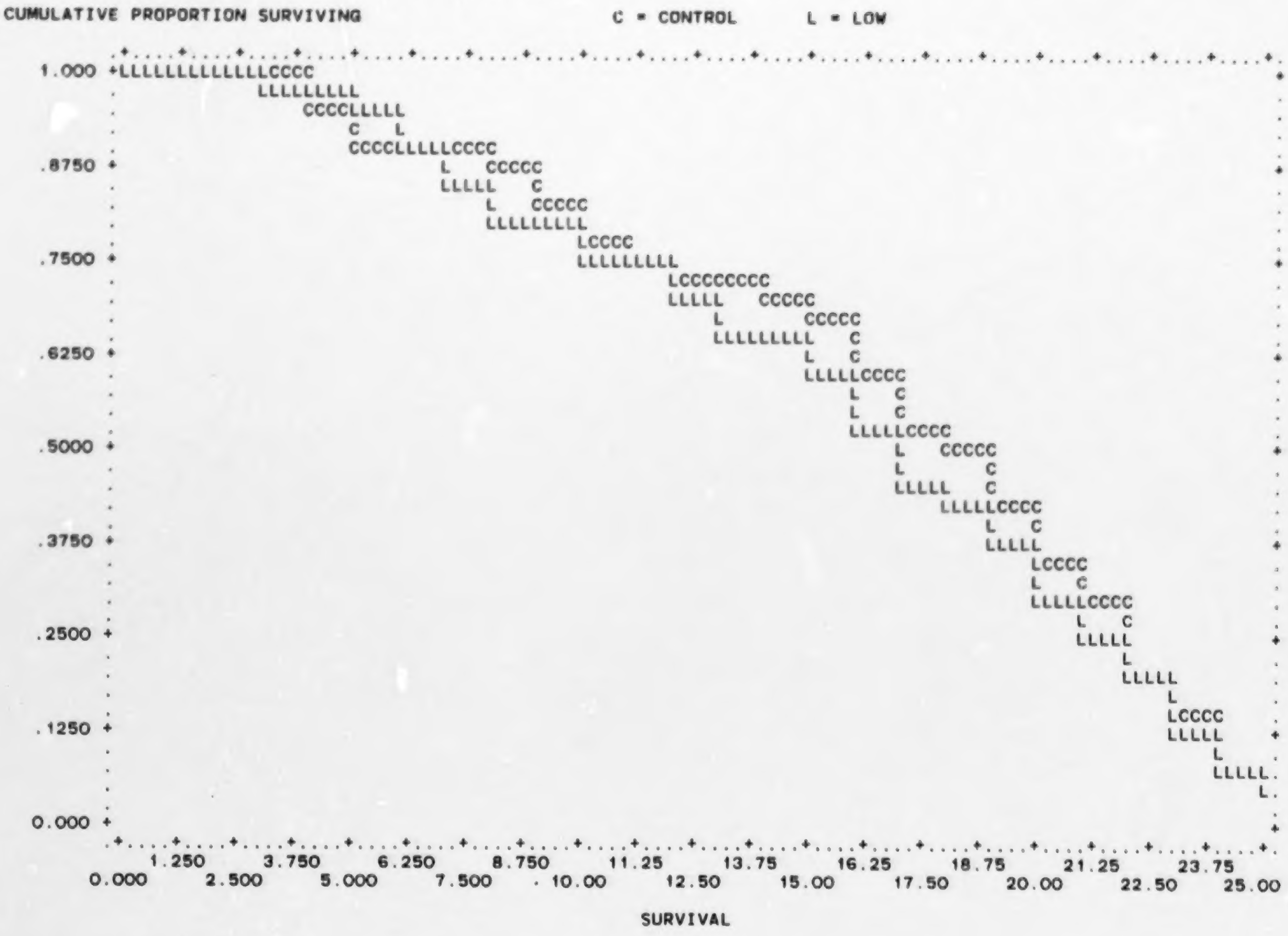
STUDY 6138 CSFO,CSFS - HIGH DOSE VS CONTROL ANALYSIS



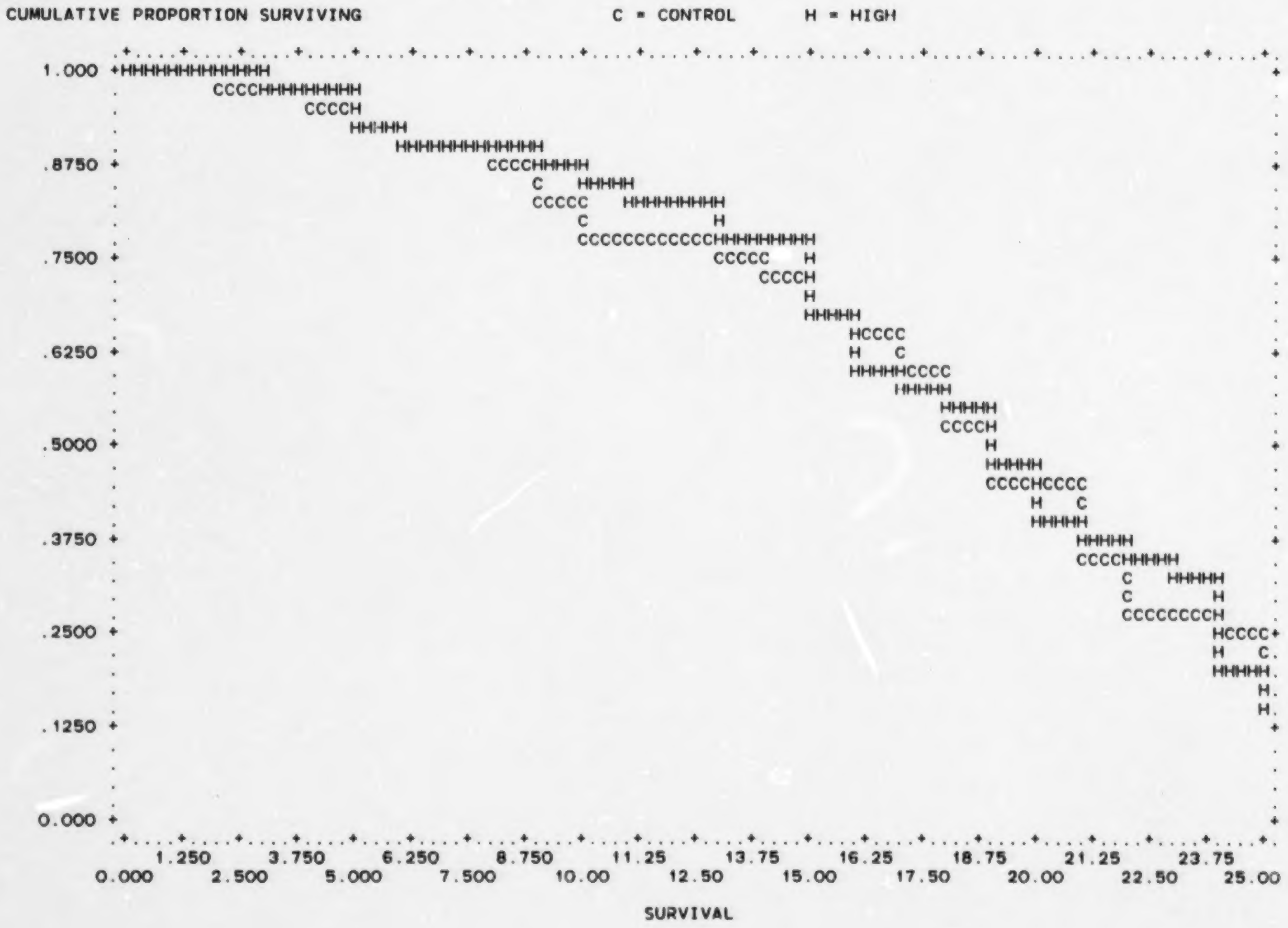
STUDY 6138 CSFO,CSFS - MED DOSE VS CONTROL ANALYSIS



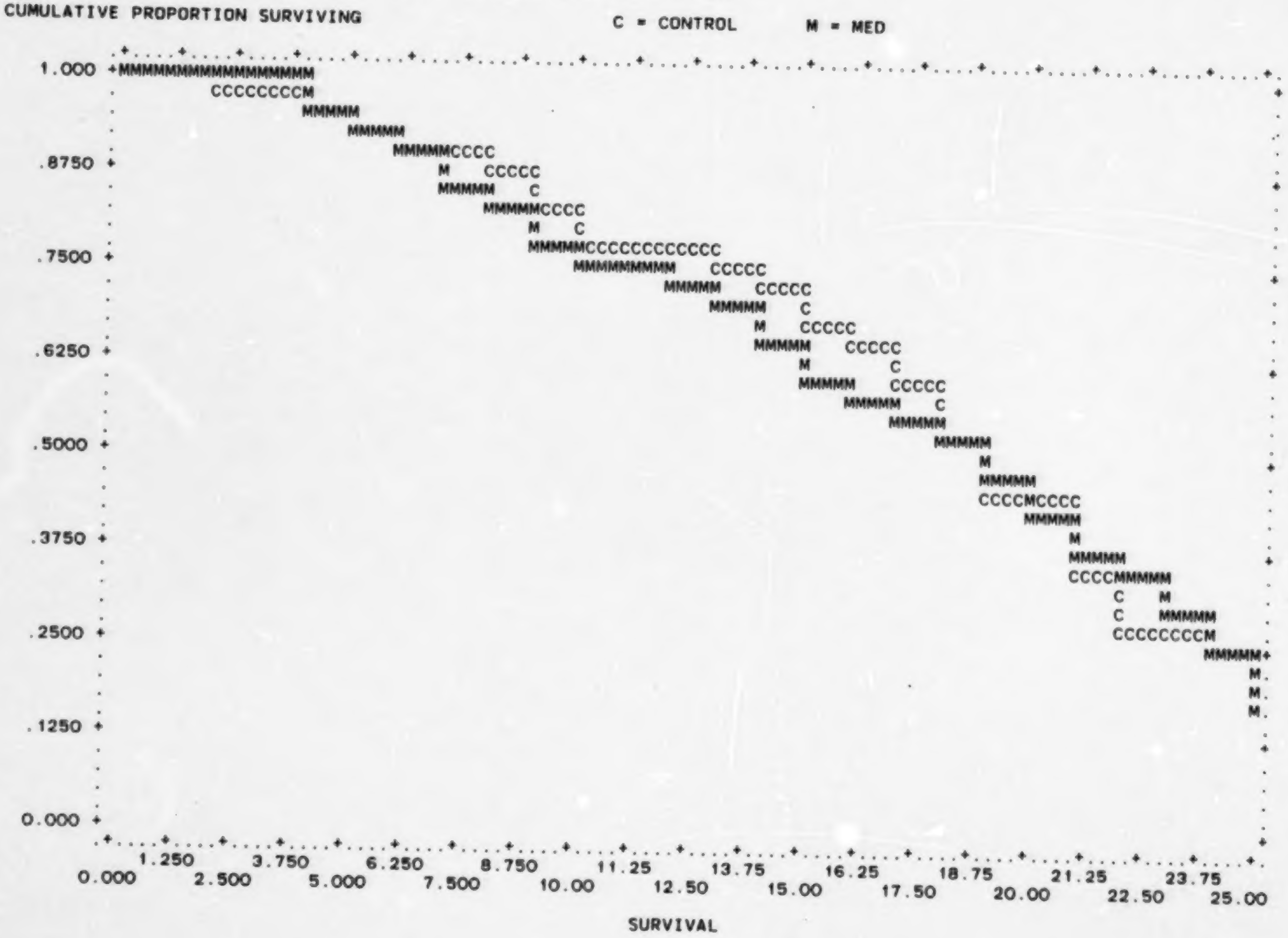
STUDY 6138 CSFO.CSFS - LOW DOSE VS CONTROL ANALYSIS



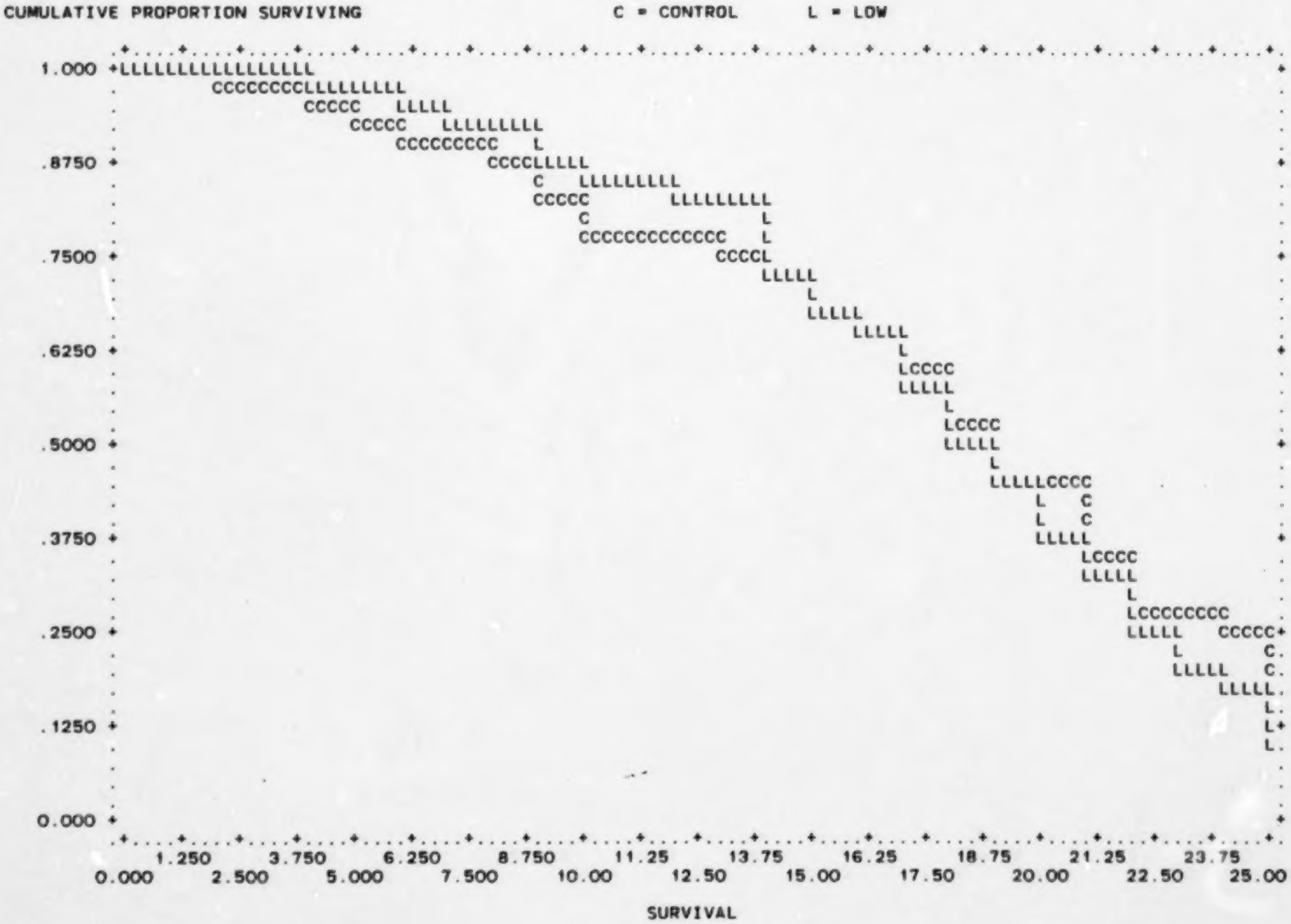
STUDY 6138 RTFO,RTFS - HIGH DOSE VS CONTROL ANALYSIS



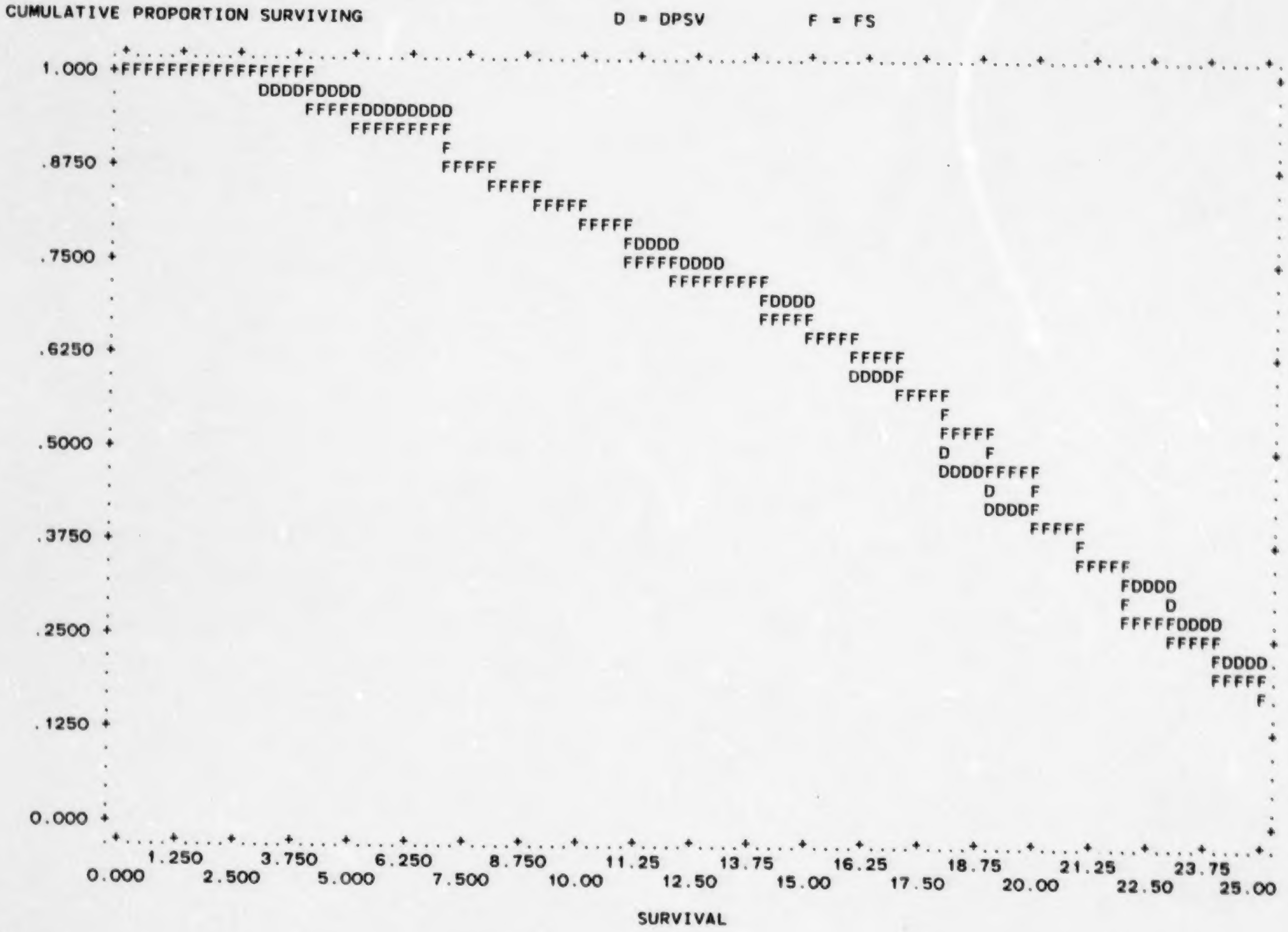
STUDY 6138 RTFO,RTFS - MED DOSE VS CONTROL ANALYSIS



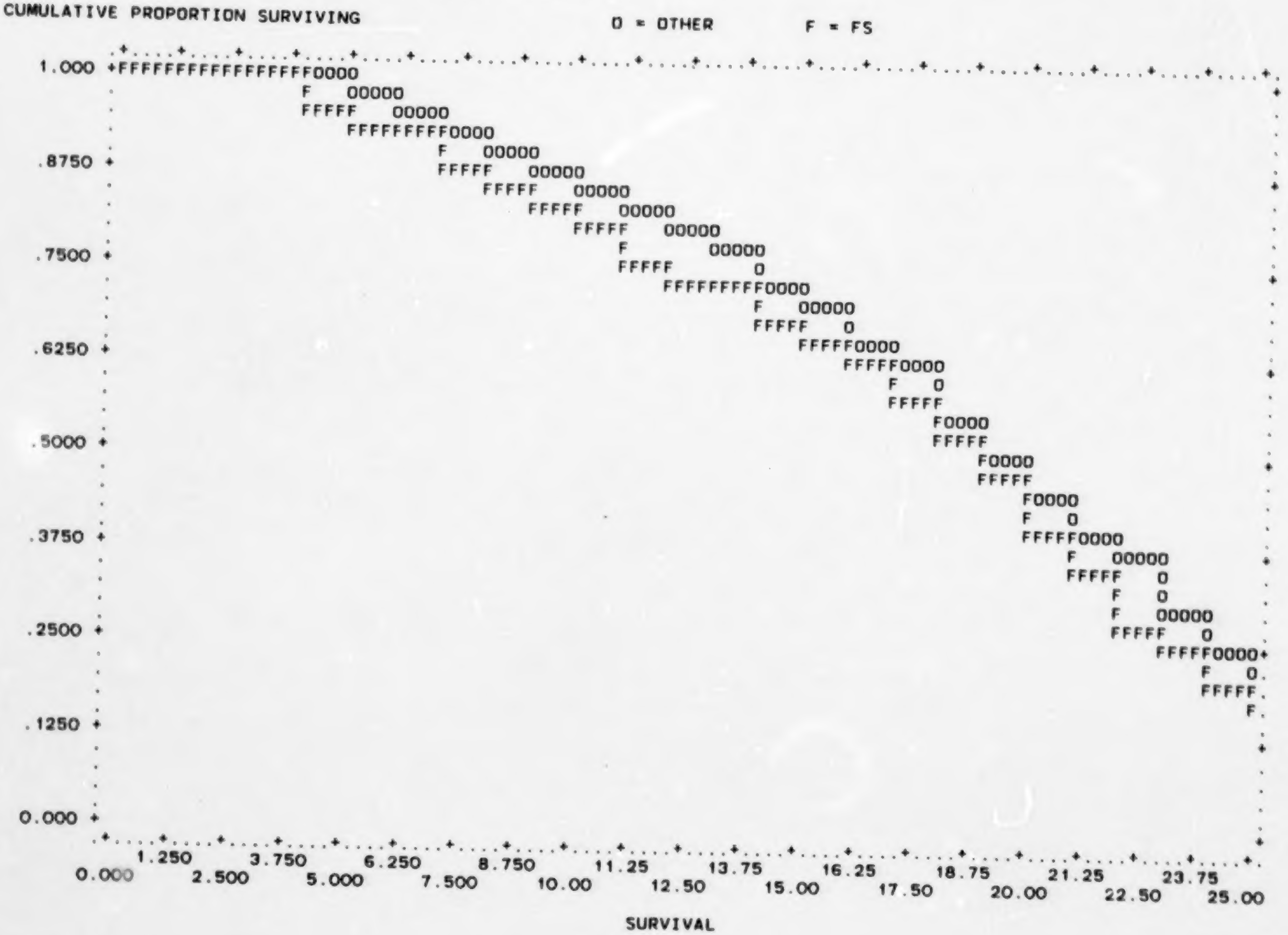
STUDY 6138 RTFO,RTFS - LOW DOSE VS CONTROL ANALYSIS



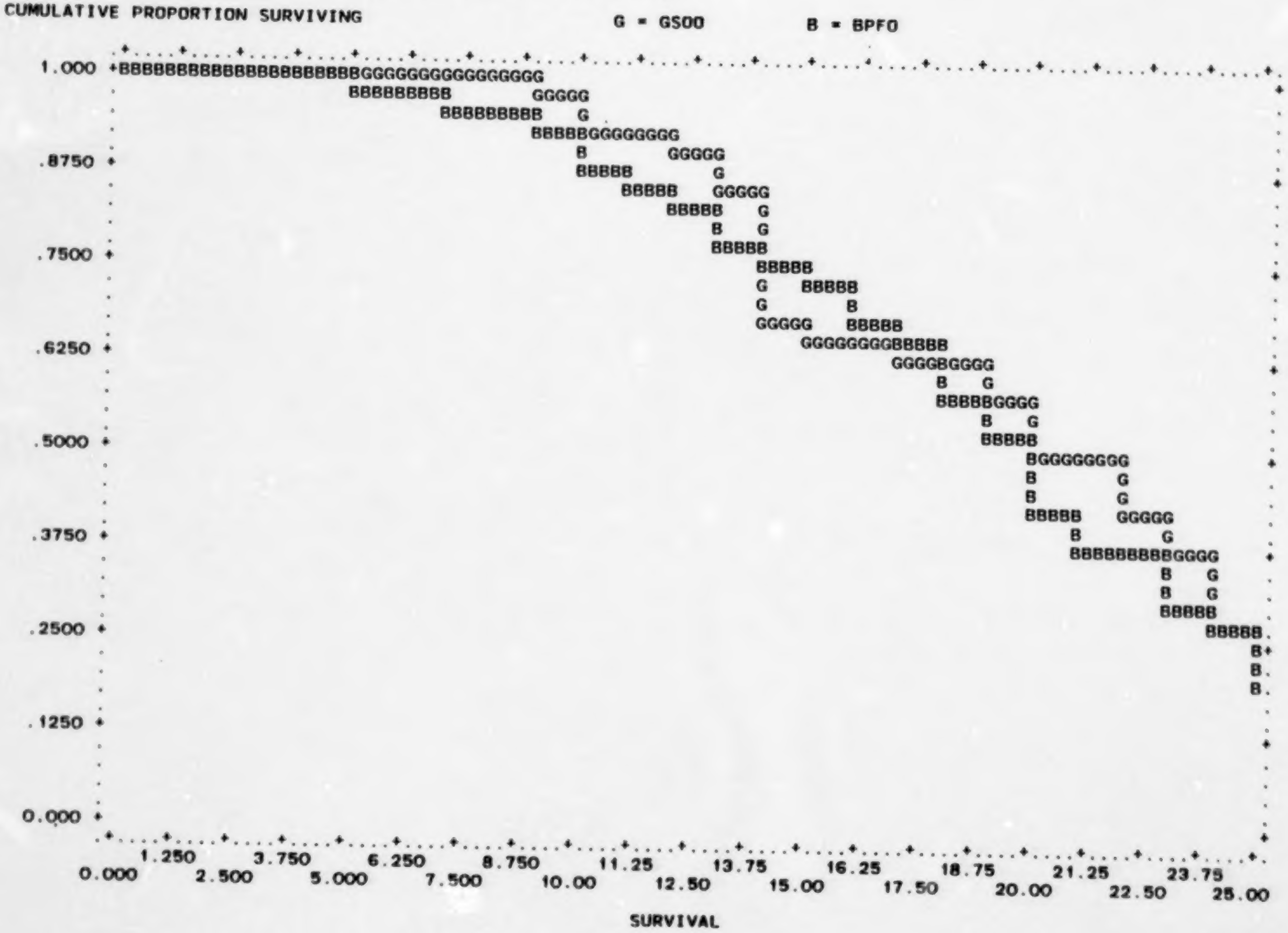
STUDY 6138 - DPSV VS ALL FS COMPOUNDS ANALYSIS



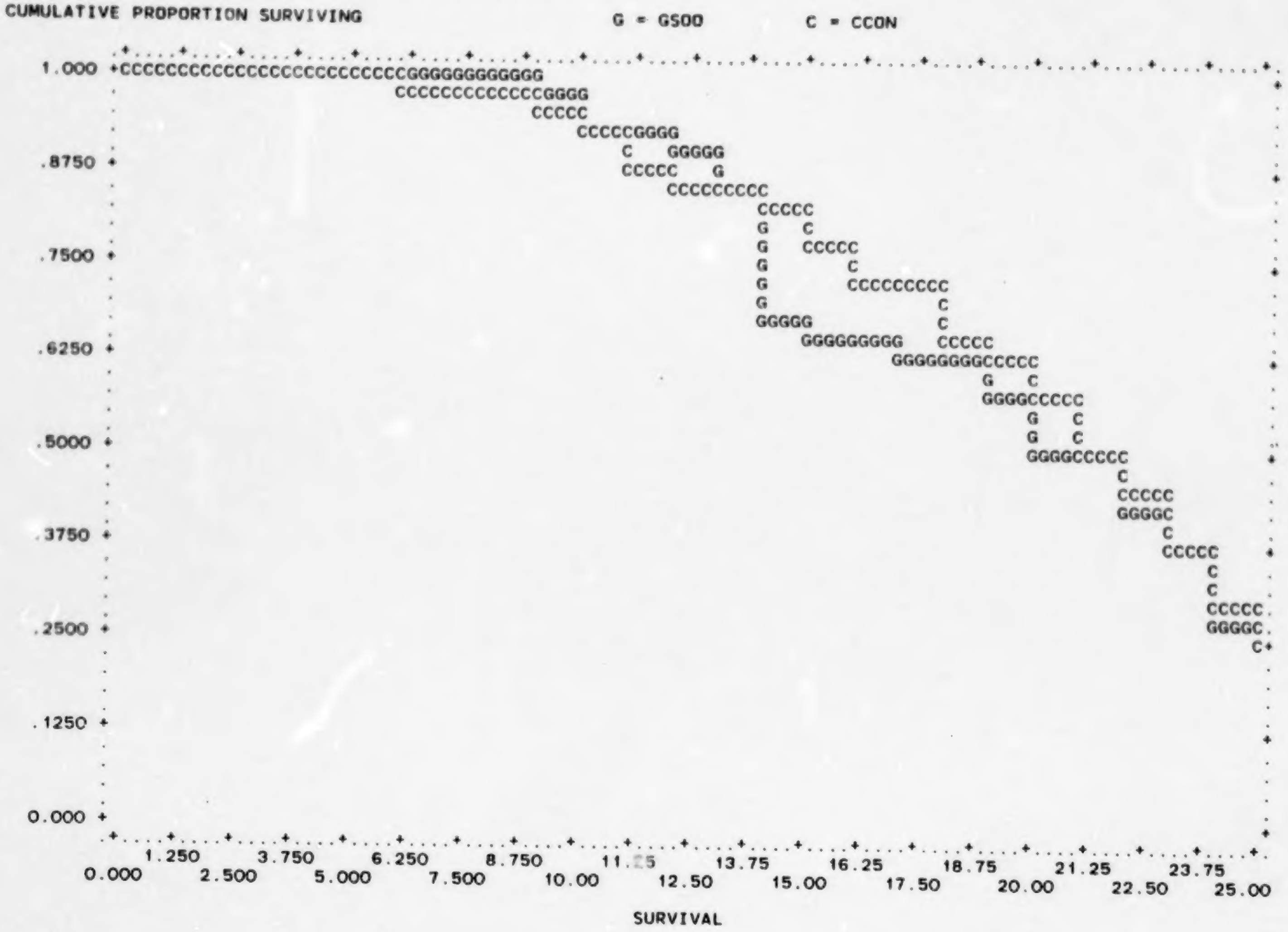
STUDY 6138 FS VS OTHER CONTROLS ANALYSIS



STUDY 6138 - GSOO (2ND REP) VS BPFO (2ND REP)



STUDY 6138 GS00 VS CCON - 2ND REPLICATION ONLY



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